A Comparison of Ultrasonic Measurement Techniques for the Maternal Cervix in the Second Trimester

Sandra O'Hara AMS DMU [1,3], Marilyn Zelesco BSc MSc AMS FIR[2], Zhonghua Sun PhD[3]

1. SKG Radiology, 30 Ord Street, West Perth, Perth, Western Australia, Australia,6005
2. Royal Perth Hospital Imaging Services, Wellington St, Perth, Western Australia, Australia, 6000.
3. Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, Perth, Western Australia, Australia, 6845

Corresponding author:

Professor Zhonghua Sun, Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, GPO Box, U1987, Perth, Western Australia 6845, Australia

Tel: +61-8-9266 7509

Fax: +61-8-9266 2377

Email: z.sun@curtin.edu.au

Short running title: Ultrasonic Techniques for the Maternal Cervix in the Second Trimester

Short running title: Ultrasonic Techniques for the Maternal Cervix in the Second Trimester

Abstract

Objectives: The aim of this study was to determine the accuracy of different ultrasound approaches for measuring the maternal cervix in patients between 17 and 22 weeks gestation.

Methods: The prospective study recruited 50 patients who were at a low risk of preterm birth. The transabdominal approach with a full bladder, post void, and transperineal approach were compared to the transvaginal approach. All measurements were acquired by one operator who was blinded to the measurements being acquired in all approaches.

Results: The transabdominal full bladder, post void, transperineal and transvaginal measurements were obtainable in 50, 49, 45 and 50 participants respectively. The mean cervical lengths were 54.58 mm, 40.74 mm, 40.60 mm and 40.54 mm respectively. These results showed nearly perfect agreement between the post void transabdominal, transperineal and transvaginal measurements with a bias of -0.06 mm and -0.16 mm from perfect agreement, respectively. The transabdominal full bladder measurements were positively biased by 14.05 mm from perfect agreement with the transvaginal approach ($p<0.05$). Forty-right of the registered transvaginal cervical lengths were greater than 25 mm and of these 47 transabdominal post void cervical lengths were equal to or greater than 30 mm, with 1 case registering 29.8 mm.

Conclusions: Transvaginal cervical length can be reproduced accurately by post void transabdominal cervical length in most cases, with a transabdominal post void cervical length of 30 mm or greater registering a transvaginal cervical length greater than 25 mm. A transperineal approach should be considered if the transvaginal approach is contraindicated.

Keywords: Cervix, preterm birth, transvaginal ultrasound, transperineal ultrasound, transabdominal ultrasound, ultrasound

Introduction

Over the last decade, little progress has been made in understanding and preventing preterm birth (PTB), and the incidence of spontaneous PTB has continued to rise, even in low risk women. [1] It has been shown that a sonographically shortened cervix is a powerful indicator of PTB in women with singleton and twin gestations - the shorter the cervical length (CL), the higher the risk of spontaneous PTB. [2]

A review of three trials performed over the last decade found that screening of CL and treatment with daily progesterone in cases of a shortened CL resulted in a reduction in PTB rates and neonatal morbidity and mortality. However it was found that 400 to 600 ultrasound examinations would be required to prevent one early PTB of less than 33 to 34 weeks gestation, and that universal screening and daily progesterone will reduce overall spontaneous delivery before 34 weeks from 2.11 to 1.85%. These studies included women with previous PTB, so the numbers may be higher in the low risk population. [3]

A recent meta- analysis concluded that the number of patients needed to be treated with vaginal progesterone rather than a placebo to prevent one case of PTB or composite perinatal morbidity/mortality before 32 weeks was 7. The corresponding numbers needed for treatment with cerclage were 10 for PTB and 11 for perinatal morbidity/mortality. [4] The cervical pessary has been shown to have a significant reduction in spontaneous delivery before 34 weeks in single and multiple gestations. [5]

The transvaginal (TV) ultrasound (US) approach is considered the 'gold standard' for measurement of CL. [6] It has been recommended that further investigation of transabdominal (TA) CL screening and determination of a threshold TA CL above which no women would have a short TV CL was needed. [3, 7, 8]

This research was developed to compare the performance of the TA pre and post void and transperineal (TP) US approaches compared to TV US for the measurement of CL during the second trimester.

Materials and Methods

Participant recruitment

The study was approved by the Institutional Review Board (IRB) and the informed consent was obtained from all patients.

Over a period of 11 months from February 2013 to January 2014, 167 women were asked to participate in this study. Of these women 12 (7.2%) were excluded from the study, 9 women (5.4%) were unable to consent due to an inability to understand the participant information and 96 (57.5%) did not consent to participate.

The 50 women (29.9%) who consented had an average age of 29 years (range 19-41). Of these 50 women 38% were in their first pregnancy, 32% in their second, 12% in their third, with the remaining ranging from their fourth to seventh pregnancy.

This was a cross-sectional study with participants from all age groups, ethnicities and socioeconomic status included in the study group. Participants of varying parities were also included in the study, with all participants at a historically low risk of PTB. The participants were between the gestations of 17 and 22 weeks of pregnancy and attending the department for their routine screening anatomy scan. Patients were excluded from the study due to the following reasons: unable to give informed consent, <18 years of age, past medical history (PMH) of preterm deliveries, PMH of cervical cerclage, PMH of cone biopsy or Large Loop Excision of the Transformation Zone (LLETZ) procedure on cervix, any cervix with suspicion of premature rupture of membranes (PROM) on the TA approach, vaginal bleeding, vaginal fluid loss, multiple gestations.

Scanning and measurement protocols

All images were acquired using the Toshiba Aplio 500 ultrasound machine. The cervix was measured initially using the TA approach with a full maternal bladder (TAF). The cervix was then measured post void using the TA approach (TAE), TP and then TV approaches. The TA approach was imaged using the 6C1 curvilinear transducer set at a transducer frequency of T4 mHz. The TP approach was imaged using the same 6C1 transducer as the TA approach, set at a transducer frequency of T3 mHz. The TV approach was imaged using the 6PV1 VT, TV transducer with a frequency of 7.3 mHz.

The TA full bladder and post void measurements were obtained with the patient in a supine position. The full bladder approach uses the maternal bladder as an acoustic window. The TA post void approach utilizes the amniotic fluid as the acoustic window. The transducer placement was slightly cephalic with a caudal tilt to visualise the cervix. The transducer was manipulated with oblique and parasagittal movements to delineate the length of the cervical canal and internal and external os.

The TP CL was obtained with the patient's hips elevated on a supportive sponge placing the patient in an elevated lithotomy position to help alleviate rectal gas overlying the external os. The transducer was placed in a sterile freezer bag and sterile gel is used as a coupling agent. The transducer was placed on the labia majora or perineum. Oblique or parasagittal movements were used to delineate the full length of the cervical canal.

The TV approach used a high frequency endovaginal transducer. The transducer was placed in a probe cover and sterile gel was used as a coupling agent. The patient was placed in the elevated lithotomy position for this approach also. The transducer was placed into the vagina on the anterior fornix of the cervix and advanced far enough to visualise the cervical canal. Oblique or parasagittal movements were used to delineate the full cervical canal. The transducer was then withdrawn till the image became out of focus and then advanced again just enough to bring the cervix back into focus. This technique was used to alleviate pressure on the cervix from the transducer that can cause artifactual lengthening of the cervical canal.

The cervix and uterus are dynamic organs that will both change in appearance throughout the ultrasound examination. The post void measurements inclusive of the TA, TP and TV approaches of the cervix were obtained in a consecutive fashion to help avoid variability in the appearance of the cervical canal due to uterine and cervical contractions. The most accurate measurement obtained in each approach was used to compare reliability of measurements.

All of these measurements were performed by an experienced sonographer with more than 20 years of experience in ultrasound imaging. The protocols were specified to achieve consistency with cervical measurements.

Measurement of cervical length

All CL measurements used a single straight line technique with calliper placement at the internal and external os for all approaches.

For all ultrasound approaches the hyperechoic cervical canal should be seen in its full length. The adjacent hypoechoic cervical glandular tissue may also be visible. The calliper placement for the internal os should be adjacent to the cervical canal at the point where the opposing sides of the cervix come together and form a flattened T-shape appearance. The calliper placement for the external os should be adjacent to the cervical canal at the point where the cervix meets the vagina. This often appears as a very slight indentation, the posterior wall of the cervix should also be used as a guide for calliper placement of the external os. [9-11] For this study in all likelihood the over-distended bladder in the TAF approach will cause the myometrium to be 'pushed' together to mimic the internal os, and this is where the calliper defining the internal os should be placed. In the TP approach the external os may be seen as a small hypoechoic 'notch' on some patients. [9, 12-14] In the TV approach the internal os may appear as a typical V-shaped notch. It may also appear as the flattened T-shape appearance. The external os is often seen with a triangular notch. [9, 12, 15]

Figures 1 to 4 are examples of calliper placement for the measurement of cervical length in the different ultrasound approaches used for this study.

Statistical analysis

Data analysis was performed using SPSS version 21.0 (SPSS V21.0, Chicago, USA). Descriptive data were presented as mean ± standard deviation (SD). All variables input to t-test procedures were first examined for normality with the Kolmogorov-Smirnov test. None was found to deviate significantly ($P < 0.05$) from normality.

The TV method was used as the reference measurement for cervical length. The other ultrasound methods were assessed for difference from the reference length. We defined any observed difference between the two measurements as measurement bias. Thus, for example (TAF-TV) represents the measurement bias attributable to the TAF method, relative to the TV standard method. Each of the test methods was assessed for bias in this way.

Bias was assessed in two ways. (1) The mean of the array of 50 differences, one difference from each participant, was compared to an ideal value of zero using a 1-sample t-test. The null hypothesis, H_0: mean bias = 0, was tested against a two-sided alternative, at the 5% level of statistical significance, ($P<0.05$). (2) Additionally, the bias values were plotted against the averages of the pairs of measured lengths using Bland-Altman plots. [16] This provides a visual indication of how the measurement bias varies, if at all, with a range of input cervical lengths in respect of both magnitude and trend.

Results

The TAF CL, TAE CL, TP CL, and TV CL measurement was obtained in 50 (100%), 49 (98%), 45 (90%), and 50 (100%) of participants, respectively.

The mean TAF CL obtained for the 50 cases was 54.58 mm (SD 10.63). The mean TV CL obtained was 40.53 mm (SD 7.76). The mean difference of TAF and TV CL was significantly different from zero with a mean difference of 14.05 mm (SE 1.25); $t_{(49)}=11.26, P<0.001$. The Bland Altman plot seen at figure 5 shows a significant positive bias of 14.05 mm for the TAF measurements away from the zero bias line in comparison to the TV measurements; this generally increases with increasing cervical length. The registered TAF and TV CL obtained for each of the 50 cases is also presented at figure 6 in the format of a scatterplot which also displays the line of equal length.

The mean TV CL and TAE CL obtained for the 49 comparable cases were 40.80 mm (SD 7.60) and 40.74 mm (SD 7.49) respectively. The mean difference of TAE and TV CL was not statistically different from zero with a mean difference of -0.06 mm (SE 0.78); $t_{(48)}$=-0.08, P=0.94. The Bland Altman plot seen at figure 7 shows a large amount of values near the zero bias line and a very slight negative bias of -0.06. The registered TAE and TV CL obtained for each of the 49 cases is also presented at figure 8 in the format of a scatterplot which also displays the line of equal length.

The mean TV CL and TP CL obtained for the 45 comparable cases were 40.76 mm (SD 7.87) and 40.60 mm (SD 7.69) respectively. The mean difference of TP and TV CL was not statistically different from zero with a mean difference of -0.16 mm (SE 0.77); $t_{(44)}$=-0.21, P=0.84. The Bland-Altman plot seen at figure 9 shows a large amount of values near the zero bias line and a very small negative bias of values of -0.16. The registered TP and TV CL obtained for each of the 45 cases is also presented at figure 10 in the format of a scatterplot which also displays the line of equal length.

Discussion

This study has three important findings. Firstly, the TAF CL overestimates cervical length by a statistically and clinically significant amount. A second finding was that the TAE CL and TP CL showed quite close correlation with the TV CL, but the TP CL was not obtainable in a significant number of cases. A third significant finding was that all TAE CL's registered at 30mm or greater registered a TV CL of greater than 25mm.

This study reports a statistically and clinically significant difference between the mean TAF CL and TV CL of 14.05 mm for the 50 cases. Our findings are consistent with those reported in the literature, with a full bladder found to overestimate CL in other studies. Hernandez-Andrade et al and Marren et al found that a cervical length obtained with a full bladder overestimated the length compared to TV CL by 8 mm and 6.1 mm respectively. [17, 18] The TAF CL can also be problematic as the cervical canal may be compressed by the bladder and 'mask' the appearance of funnelling of the cervical canal due to premature rupture of membranes. [9]

There was a small difference between the mean TV CL and TAE CL of -0.06 mm for this study. Other studies also found that the mean TAE CL was shorter than TV CL, these studies reported the mean TAE CL was -2.82, -2.5 and -2.6 mm different respectively. [7, 19, 20] Marren et al found a mean difference of 0.6 mm between TAE and TV CL. [18]

The TAE CL was registered in 98% of cases in this research. Stone et al were able to measure the TAE CL in 100% of cases as were Saul et al.[11, 19] Studies by Marren et al and Friedman et al were able to register measurements for TAE CL in 82.8% and 82.1% of patients respectively. [7, 18] Marren et al used the same guidelines for measuring the TAE CL as the TV CL, and this may be a reason for this difference in registered TAE CL's. Freidman et al stated that the majority of patients in their study were overweight, obese or morbidly obese.

There have been recommendations made by other researchers that there is a need for an established 'cut off' point where we can be confident that if the TA CL obtained is above a certain length that we can be confident that the TV CL would be greater than 25 mm. Stone et al suggested that if the TAE CL was 25 mm or greater there would be little to be gained by TV scanning in the low risk population.[19] Freidman et al concluded that a TA CL of 35 mm or greater would need to be obtained to be confident that the TV CL would be greater than 25 mm, this included TA CL acquired with a full bladder.[7] Marren et al concluded that a policy of routinely performing the TA CL and proceeding to TV with a TAE CL <25 mm would miss 67% of cases with a shortened CL.[18]

This study only yielded two TV CL measurements less than 30 mm, the shortest TV CL obtained was 22.6 mm, and for this case the registered TAE CL was 18.5 mm. The one case in this study that could not be measured using the TAE approach was the second shortest measurement obtained with a TV CL of 27.6 mm. This resulted in 49 of the 50 cases (98%) of TV CL obtained having a CL of equal to or greater than 25 mm, and of these 48 (97.9%) registered a TAE CL equal to or greater than 30 mm, with the remaining case having a TAE CL of 29.8 mm. Saul et al found that a post void TA cervical length cut off of 30 mm or less showed 100% sensitivity for identifying cervices with lengths of 25 mm or less on TV sonography.[11] In our results on low risk women in all patients with a TAE CL of 30 mm or greater a corresponding TV CL of 29.8 mm or greater was registered.

This study reports a difference of -0.16 mm between the mean TV and TP CL, but TP CL was only obtainable in a statistically significant 90% of cases. These results are similar to Cicero et al who also looked at the cervix using the TP approach in the mid trimester (22-24 weeks). [14] They showed a mean difference in CL of 0.2 mm between TV and TP CL, though were only successful in 80% of patients. Yazici et al showed a mean CL difference of 1mm between TP and TV approaches and were successful in measuring the TP CL in 89% of patients. [21]

Sonographer training and experience is a key factor in obtaining diagnostic images in all ultrasound approaches. The TA approach performed post void appears to be more successful in obtaining a CL than the TP approach. The TV approach is technically easier to obtain in most patients, but experience is also required to utilise the correct technique and recognise key landmarks.

This study has some limitations that should be acknowledged. First, the sample size is quite small, as the acceptance rate to participate in the study is relatively low. Furthermore, it is based on a single centre experience. It was also limited as excluding the women who were unable to consent for this study, 34% of women agreed to participate in this study with 66% not agreeing.

In conclusion, the cervix should not be assessed with a full maternal bladder due to overestimation of CL. The TP approach is unsuccessful in a significant number of cases even with an experienced sonographer, and should be utilised if the TV approach is contraindicated. The poor acceptance rate of women to undertake the TP and TV approaches, and the close correlation of TAE CL to TV CL warrants further investigation into the use of TAE CL as a screening tool for PTB with standardisation of accepted landmarks and establishment of a standard TAE CL above which all TV CL will be greater than 25mm.

Acknowledgements

We would like to thank Ms Karen Rocke and Ms Emmeline Lee for their assistance in this study. Our great appreciation is given to Mr Gil Stevenson for his kind help with statistical analysis.

References

1. Chandiramani M, Shennan AH. Premature cervical change and the use of cervic al cerlage. *Fetal Matern Med Rev* 2007; 18 : 25-52.
2. Romero R, Nicolaides K, Conde-Agudelo A, et al. Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and meta analysis of individual patient data. *Am J Obstet Gynecol* 2012; 206 :124.e1-e19.
3. Parry S, Simhan H, Elovitz M, Iams J. Universal maternal cervical length screening during the second trimester: pros and cons of a strategy to identify women at risk of spontaneous preterm delivery. *Am J Obstet Gynecol* 2012; 207: 101-106.
4. Conde-Agudelo A, Romero R, Nicolaides K, et al. Vaginal progesterone vs cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: A systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013; 208 :42. e1-e18.
5. Di Tommaso M, Berghella V. Cervical length for the prediction and prevention of preterm birth. *Expert Review Obstet Gynecol* 2013; 8 :345-355.
6. Bergelin I, Valentin L. Normal cervical changes in parous women during the second half of pregnancy – a prospective, longitudinal ultrasound study. *Acta Obstet Gynecol Scand* 2002; 81 :31-38.

7. Friedman AM, Srinivas SK, Parry S, Elovitz MA, Wang E, Schwartz N. Can transabdominal ultrasound be used as a screening test for short cervical length? *Am J Obstet Gynecol* 2013; 208 :190. e1-e7.
8. Miller ES, Grobman WA. Cost-effectiveness of transabdominal ultrasound for cervical length screening for preterm birth prevention. *Am J Obstet Gynecol* 2013; 209 :546.e1-e6.
9. Rumack CM, Wilson SR, Charboneau W, Levine D. Diagnostic Ultrasound. 4th ed. Philadelphia: Elsevier Mosby; 2011.
10. Andersen HF, Nugent CE, Wanty SD, Hayashi RH. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. *Am J Obstet Gynecol* 1990; 163 :859-867.
11. Saul LL, Kurtzman JT, Hagemann C, Ghamsary M, Wing DA. Is transabdominal sonography of the cervix after voiding a reliable method of cervical length assessment? *J Ultrasound Med* 2008; 27 :1305-1311.
12. Callen PW. Ultrasonography in Obstetrics and Gynaecology. 5th ed. Philadelphia: Saunders Elsevier; 2008.
13. Meijer-Hoogeveen M, Stoutenbeek P, Visser GH. Transperineal versus transvaginal sonographic cervical length measurement in second- and third-trimester pregnancies. *Ultrasound Obstet Gynecol* 2008; 32 :657-62.
14. Cicero S, Skentou C, Souka A, To MS, Nicolaides KH. Cervical length at 22-24 weeks of gestation: comparison of transvaginal and transperineal-translabial ultrasonography. *Ultrasound Obstet Gynecol* 2001; 17 :335-40.
15. Nicholaides K. Fetal Medicine Foundation: Cervical Assessment on line Course In: Fetal Medicine Foundation. Fetal Medicine Foundation; 2012.

16. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307-310.
17. Hernandez-Andrade E, Romero R, Ahn H, et al. Transabdominal evaluation of uterine cervical length during pregnancy fails to identify a substantial number of women with a short cervix. *J Matern Fetal Neonatal Med* 2012; 25: 1682-1689.
18. Marren AJ, Mogra R, Pedersen LH, Walter M, Ogle RF, Hyett JA. Ultrasound assessment of cervical length at 18–21 weeks' gestation in an Australian obstetric population: Comparison of transabdominal and transvaginal approaches. *Aust N Z J Obstet Gynaecol* 2014; 54: 250-255.
19. Stone PR, Chan EHY, McCowan LME, Taylor RS, Mitchell JM; SCOPE Consortium. Transabdominal scanning of the cervix at the 20-week morphology scan: Comparison with transvaginal cervical measurements in a healthy nulliparous population. *Aust N Z J Obstet Gynaecol* 2010; 50 :523-527.
20. To MS, Skentou C, Chan C, Zagaliki A, Nicolaides KH. Cervical assessment at the routine 23-week scan: standardizing techniques. *Ultrasound Obstet Gynecol* 2001; 17 :217-219.
21. Yazici G, Yildiz A, Tiras MB, Arslan M, Kanik A, Oz U. Comparison of transperineal and transvaginal sonography in predicting preterm delivery. *J Clin Ultrasound* 2004; 32 :225-230.

Conflicts of interest

We declare that there is no conflict of interest in this study.

Figures and figure legends

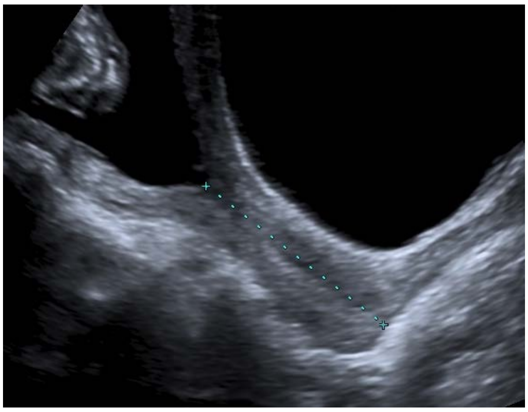

Figure 1 is an example of a TA measurement of cervical length with a full bladder.

Figure 2 is an example of a TA cervical length measurement post void.

Figure 3 is an example of measurement of cervical length using the TP approach.

Figure 4 is an example of measurement of cervical length using the TV approach.

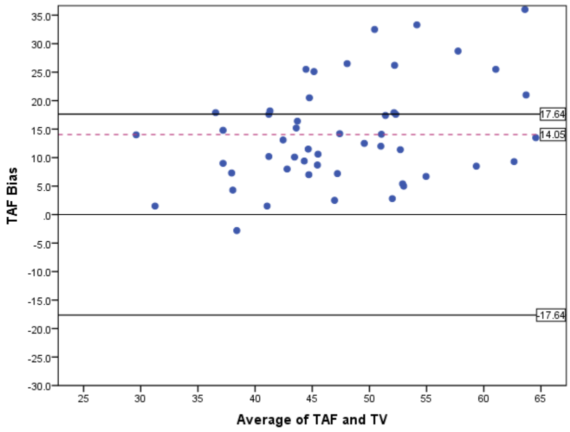

Figure 5: Bland-Altman plot of TAF vs TV bias, showing line of mean bias (14.05 mm) and 95% tolerance limits about zero bias.

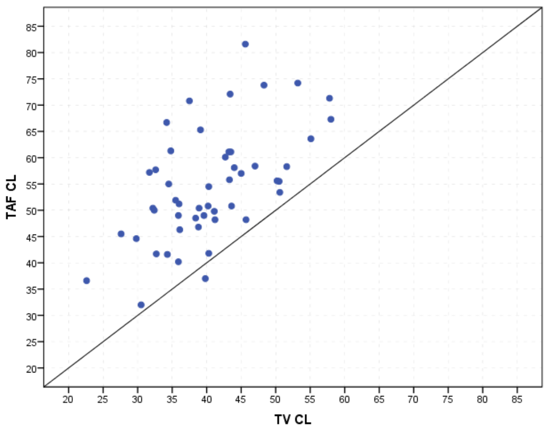

Figure 6: Scatterplot of TAF vs TV CL showing line of equal length.

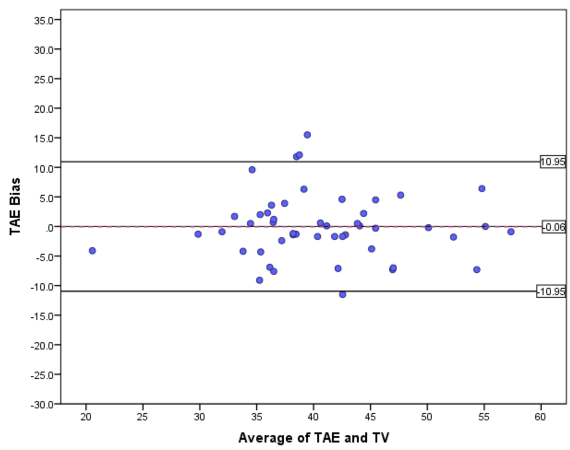

Figure 7: Bland-Altman plot of TAE vs TV bias, showing line of mean bias (-0.06 mm) and 95% tolerance limits about zero bias.

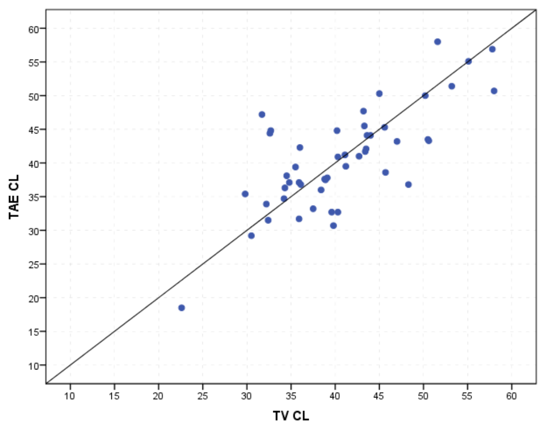

Figure 8: Scatterplot of TAE vs TV CL showing line of equal length.

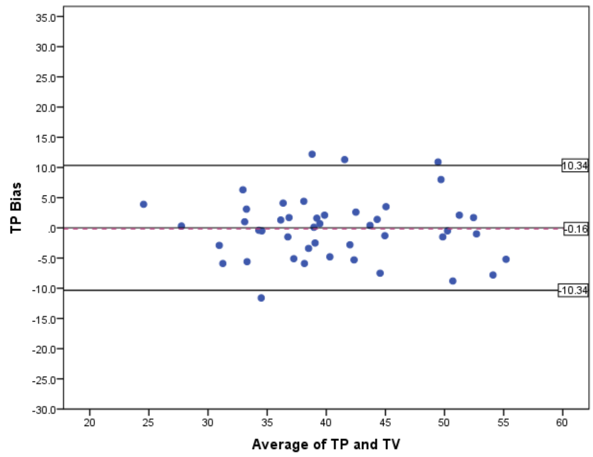

Figure 9: Bland-Altman plot of TP vs TV bias, showing line of mean bias (-0.16 mm) and 95% tolerance limits about zero bias.

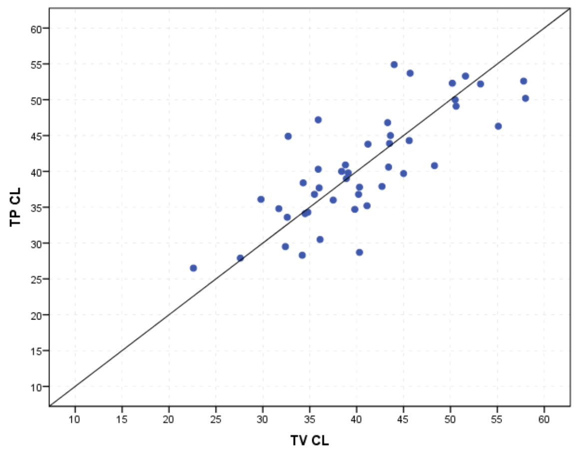

Figure 10: Scatterplot of TP vs TV CL showing line of equal length.