Comparison of magnetic resonance imaging to ultrasound for prostate sizing

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Introduction: *To compare pelvic ultrasound (PUS) and transrectal ultrasound (TRUS) to magnetic resonance imaging (MRI) in the estimation of prostate size.*

Materials and methods: *After IRB approval, we performed a single-center, retrospective study of 91 patients who had prostate sizing between August, 2013 and June, 2017. Correlation, reliability, and agreement between PUS, TRUS, and MRI were calculated through the Pearson coefficient, intraclass correlation coefficient, and Bland-Altman analysis, respectively. Data was stratified by prostate size, body mass index, and time between imaging acquisition.*

Results: *A total of 91 patients underwent all three imaging methods. Median age was 64, median body mass index (BMI) was 27 kg/m^2, and median PSA value prior to PUS was 7.1 ng/mL. Pearson coefficient for MRI versus TRUS and MRI versus PUS was 0.90 and 0.87, respectively. Intraclass correlation coefficient was 0.90 (0.87-0.93) comparing all three modalities. BA analysis for MRI versus TRUS and MRI versus PUS showed that for prostates ≤ 50 cc, greater than 79% of the data fell within limits of agreement. Percentages decreased with increasing prostate size to 46% and 41% for prostates > 50 cc and ≤ 80 cc and to 28% and 25% for prostates > 80 cc for MRI versus TRUS and MRI versus PUS, respectively.*

Conclusions: *MRI may be considered clinically interchangeable with TRUS and PUS for prostate sizing at prostate volumes ≤ 50 cc. For larger prostates and when minor changes in prostate size would drastically alter surgical management, cross-sectional imaging should be considered.*

Key Words: prostatic hyperplasia, magnetic resonance imaging

Introduction

Prostate size is important in managing both benign prostatic hyperplasia (BPH) and prostate cancer. AUA guidelines for surgical management of BPH now include consideration of prostate volume measurement prior to intervention.[1] There are several surgical options for men with lower urinary tract symptoms and prostate volume helps to stratify the choice of intervention.

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In addition to BPH, prostate size can influence management decisions in prostate cancer. Multiple studies have found smaller prostates to be associated with higher grade disease when compared to larger glands.[2,3] Aizer et al found a higher incidence of severe acute genitourinary toxicity in patients undergoing intensity-modulated radiation therapy with larger prostates.[4] For patients undergoing brachytherapy, sizing helps identify patients with large prostates who may benefit from pre-treatment androgen deprivation therapy to reduce volume.[5]

When measuring prostate size, ultrasound (US) is quick, inexpensive, accessible, and radiation-free. Transrectal ultrasound (TRUS) is widely utilized for sizing of the prostate and has been demonstrated to be comparable to excised cadaveric weight in measuring prostate size.[6] Although accurate, TRUS is invasive,

more uncomfortable to patients, and takes longer to perform than transabdominal pelvic ultrasound (PUS). In a previous study by our group, Pate et al, we found that although there was good correlation between TRUS and PUS, the two were only interchangeable for prostates smaller than 30 cc.[7] Though measurement of the prostate with MRI was first attempted in the 1980s, technological advancements over the last decade have led to widespread use of MRI in the diagnosis and pre-treatment planning of men with suspected or biopsy-proven prostate cancer.[8] In addition to identifying clinically suspicious lesions, local invasion, or lymphadenopathy, prostate volume and anatomy can be easily measured.[9] A number of studies have assessed prostatic volume measured by MRI and found it to be accurate when compared to surgical specimens.[10] Others have compared MRI and TRUS, the overwhelming majority of whom have deemed the two modalities to be comparable, and conclude that both may be effectively used when estimating prostate size.[9,11-18] Some noted differences in the two modalities or suggested that MRI overestimated volume compared to TRUS.[17,19] There is a paucity of data comparing PUS to MRI.

Prostate volume plays an important role in the treatment of prostatic disease. Multiple imaging modalities are available to size the prostate, each with varying costs, availability, speed, accuracy, and comfort. Given the advantages of pelvic ultrasound, we sought to compare the accuracy of MRI to prostate ultrasound (both PUS and TRUS) in the estimation of prostate size in a large, diverse cohort of men at our institution.

Materials and methods

After IRB approval, we performed a single-center, retrospective study of 91 patients with PUS, TRUS, and MRI imaging for prostate sizing between August 15, 2013 and June 20, 2017. Time between prostate imaging exams was limited to a maximum of 4 years, and patients with interval procedures that could modify prostate volume, including prostate radiation and resection, were excluded. The vast majority of ultrasound measurements were performed by our experienced in-house ultrasonographer, with only a few by an attending urologist with ultrasound certification. PUS was performed transabdominally with the patient instructed to attend clinic with a full bladder. All MRI images were read by a single radiologist. In cases where multiple images were recorded with one modality, only those with the shortest time-span between different modalities were analyzed. Patient age, race, BMI, PSA, prostate biopsy results, and use of alpha-blocker or 5-alpha reductase inhibitor.

Prostate volumes for both prostate ultrasound as well as MRI were derived from ellipsoid volume calculation (length×width×height×π/6) using dimensions recorded with ultrasound (Prosound a6 by Aloka) and MRI. Correlation between MRI versus TRUS and PUS was calculated through the Pearson coefficient (PC). Reliability was analyzed through interrater reliability analysis using the intraclass correlation coefficient (ICC) as a reliability index. A p value of $p < 0.05$ was used to determine statistical significance.

In addition to calculating correlation, we utilized Bland-Altman (BA) analysis to measure agreement between MRI and each of the ultrasound imaging methods (MRI versus TRUS and MRI versus PUS). While linear regression models evaluate whether two measurements are related, BA analysis is preferred in evaluation of agreement, as it is possible for two methods to demonstrate a strong correlation without agreement. BA analysis plots the mean of the measurements recorded by the two imaging methods being compared on the x-axis against the difference between the same two measurements on the y-axis. There are also plotted lines on the graph that represent the 95% confidence interval to visualize how much of the patient data fits within these limits. This interval is also known as the limits of agreement (LOA). As has been done in other studies we included our own predetermined acceptable range, which we refer to as clinical limits of agreement, that helps frame the data in a clinical context.[20] In this study we set the clinical limits of agreement at ± 10 cc from the mean difference between volume estimates by different imaging modalities. We also include data with clinical limits of agreement set at ± 5 cc and ± 20 cc to capture ranges that different practitioners may deem acceptable.

Results

A total of 299 male patients underwent transrectal ultrasound and prostate needle biopsy for either an elevated PSA or abnormal digital rectal exam. Of these patients, 91 had MRI, TRUS, and PUS imaging performed and met inclusion criteria. Eighty four percent of patients had an MRI within 2 years of PUS and 86% of patients had an MRI within 2 years of TRUS. Demographic data for patients with all three imaging modalities performed is summarized in Table 1. The median age was 64 (49-80) years old, median BMI was 27 kg/m^2, and median PSA value prior to PUS was 7.1 ng/mL. Eighteen (20%) patients were White, 39 (43%) were Black, and 21 (23%) were Hispanic. The

TABLE 1. **Patient characteristics**

Total number of patients	91
Median age (years)	64
Median PSA (ng/mL)	7.1
Median prostate size (cc)	
Measured by TRUS (cc)	50
Measured by PUS (cc)	50
Measured by MRI (cc)	43
No. race (%)	
Black	39 (43)
White	18 (20)
Hispanic	21 (23)
Asian	1 (1.1)
Other/unknown	12 (13)
No. time between TRUS and MRI (%)	
≤ 1 year	64 (70)
> 1 to ≤ 2 years	15 (16)
> 2 to ≤ 3 years	6 (6.6)
> 3 to ≤ 4 years	6 (6.6)
No. BMI (%)	
≤ 25 kg/m^2	23 (24.5)
> 25 to ≤ 30 kg/m^2	39 (41.5)
> 30 kg/m^2	19 (20.2)
Not recorded	13 (13.8)
Median BMI (kg/m^2)	27
No. prostate size by PUS (%)	
≤ 30 cc	18 (20)
> 30 to ≤ 50 cc	29 (32)
> 50 to ≤ 80 cc	28 (31)
> 80 cc	16 (18)
No time between PUS and MRI (%)	
≤ 1 year	59 (65)
> 1 to ≤ 2 years	17 (19)
> 2 to ≤ 3 years	9 (10)
> 3 to ≤ 4 years	6 (7)

median prostatic volume was 50 (18-215) cc for TRUS, 50 (17-239) cc for PUS, and 43 (12-221) cc for MRI. Median lobe was only noted on imaging for 17 (19%) patients, though precise volumes were not recorded. Mean difference in prostate volume between MRI and TRUS ($Vol_{TRUS} - Vol_{MRI}$) was (-6.8 ± 15) cc, and mean difference in volume between MRI and PUS ($Vol_{PUS} - Vol_{MRI}$) was (-5.3 ± 16) cc. PC for MRI versus TRUS was 0.90, and PC for MRI versus PUS was 0.87, Figure 1. The ICC was 0.90 (0.87-0.93) comparing all three modalities, 0.90 (0.85-0.93) for MRI versus TRUS, and 0.87 (0.81, 0.91) for MRI versus PUS, Table 2.

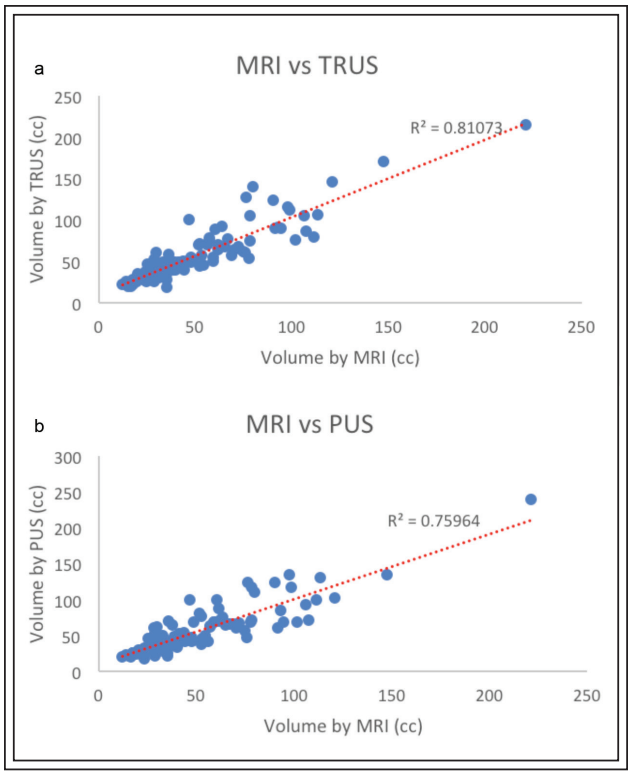

Figure 1. Prostate volume measured by MRI compared to prostate volume measured by TRUS and PUS.

BA analysis for MRI versus TRUS showed that for all patients, 57% of the data fell within clinical LOA of ± 10 cc, 35% within clinical LOA of ± 5 cc, and 84% within clinical LOA of ± 20 cc, Figure 2. When stratified by prostate size, BA analysis for MRI versus TRUS showed that in prostates ≤ 30 cc by TRUS, 86% of the data fell within clinical LOA of ± 10 cc, 57% within clinical LOA of ± 5, and 100% within clinical LOA of ± 20%, Table 3, Figures 3-5. For prostates > 30 cc and ≤ 50 cc, 82% of the data fell between clinical LOA of ± 10%, 50% within clinical LOA of ± 5%, and 100% within clinical LOA of ± 20%. For prostates > 50 cc and ≤ 80 cc 46% of the data fell between clinical LOA of ± 10 cc, 20% within clinical LOA of ± 5 cc, and 80% within clinical LOA ± 20 cc. For prostates > 80 cc 28% of the data fell between clinical LOA of ± 10 cc, 17% within clinical LOA ± 5 cc, and 61% within clinical LOA of ± 20 cc.

BA analysis for MRI versus PUS showed that for all patients, 47% of the data fell within clinical LOA of ± 10 cc, 41% within clinical LOA of ± 5 cc, and 77% within clinical LOA of ± 20 cc, Table 3, Figures 6-8. When stratified by prostate size, BA analysis for MRI versus PUS showed that in prostates ≤ 30 cc by TRUS, 89% of the data fell within clinical LOA of

TABLE 2. **Pearson (PC) and intraclass correlation coefficients (ICC) stratified by body mass index and time between imaging exams**

	TRUS vs. MRI		PUS vs. MRI		TRUS vs. PUS vs. MRI
	PC	ICC (CI)	PC	ICC (CI)	ICC (CI)
Overall	0.90	0.90 (0.85-0.93)	0.87	0.87 (0.81-0.91)	0.90 (0.87-0.93)
BMI					
≤ 25 kg/m^2	0.93	0.95 (0.87-0.98)	0.92	0.92 (0.81-0.97)	0.95 (0.89-0.97)
> 25 to ≤ 30 kg/m^2	0.89	0.84 (0.71-0.92)	0.89	0.86 (0.74-0.93)	0.85 (0.76-0.91)
> 30 kg/m^2	0.89	0.92 (0.82-0.96)	0.88	0.84 (0.66-0.93)	0.90 (0.81-0.95)
Time between exams					
≤ 1 year	0.92	0.92 (0.87-0.95)	0.89	0.89 (0.83-0.94)	
> 1 to ≤ 2 years	0.83	0.81 (0.53-0.93)	0.75	0.74 (0.42-0.90)	
> 2 to ≤ 3 years	0.89	0.80 (0.13-0.97)	0.94	0.85 (0.46-0.96)	
> 3 to ≤ 4 years	0.73	0.73 (0.05-0.96)	0.88	0.82 (0.18-0.97)	

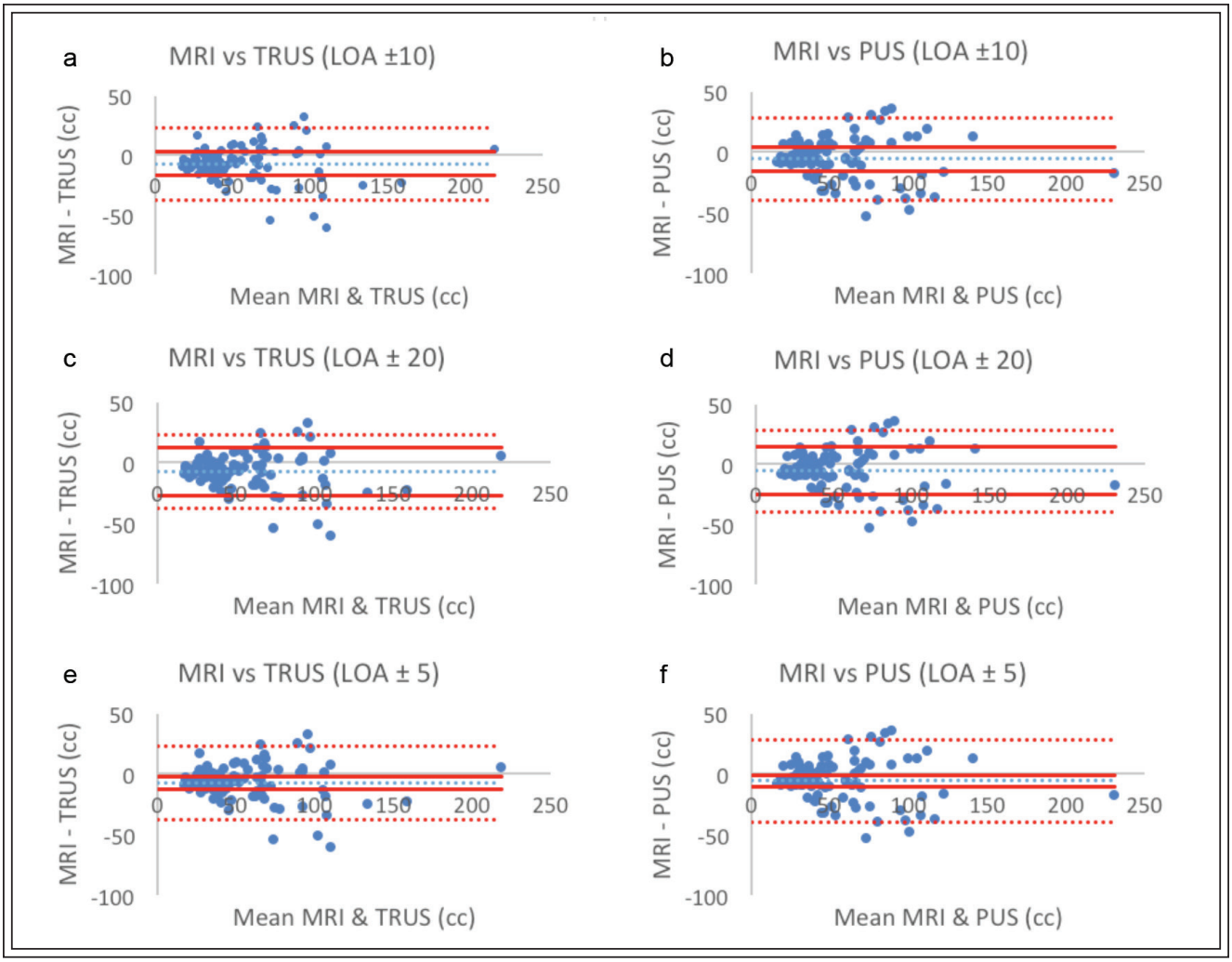

Figure 2. Bland-Altman analysis comparing average volume as recorded by US and MRI to the difference between volume measurements.

TABLE 3. **Proportion of patients for which the difference between prostate volume estimate by ultrasound and magnetic resonance imaging fell within clinical limits of agreement of ± 10 cc, ± 5 cc, and ± 20 cc**

	(MRI-TRUS) within clinical limits of agreement			(MRI-PUS) within clinical limits of agreement		
Prostate size (US)	**LOA ± 10**	**LOA ± 5**	**LOA ± 20**	**LOA ± 10**	**LOA ± 5**	**LOA ± 20**
≤ 30 cc	86%	57%	100%	89%	39%	100%
> 30 to ≤ 50 cc	82%	50%	100%	79%	44%	97%
> 50 to ≤ 80 cc	46%	20%	80%	41 %	18%	64%
> 80 cc	28%	17%	61%	25%	19%	44%

± 10 cc, 39% within clinical LOA of ± 5 cc, and 100% within clinical LOA of ± 20 cc. For prostates > 30 cc and ≤ 50 cc, 79% of the data fell between clinical LOA of ± 10 cc, 44% within clinical LOA of ± 5 cc, and 97% within clinical LOA of ± 20 cc. For prostates > 50 cc and ≤ 80 cc 41% of the data fell between clinical LOA of ± 10 cc, 18% within clinical LOA of ± 5 cc, and 64% within clinical LOA of ± 20 cc. For prostates > 80 cc, 25% of the data fell between clinical LOA of ± 10 cc, 19% within clinical LOA of ± 5 cc, and 44% within clinical LOA of ± 20 cc.

Discussion

We found a strong positive correlation between TRUS and MRI measurements of prostate volume (R = 0.90), which is consistent with prior studies that found correlation ranged from 0.8-0.9.[14,19,21] We found strong positive correlation between PUS and MRI (R = 0.87) but we could not find any prior studies comparing these two modalities.

Interrater reliability analysis demonstrated borderline good to excellent reliability when analyzing

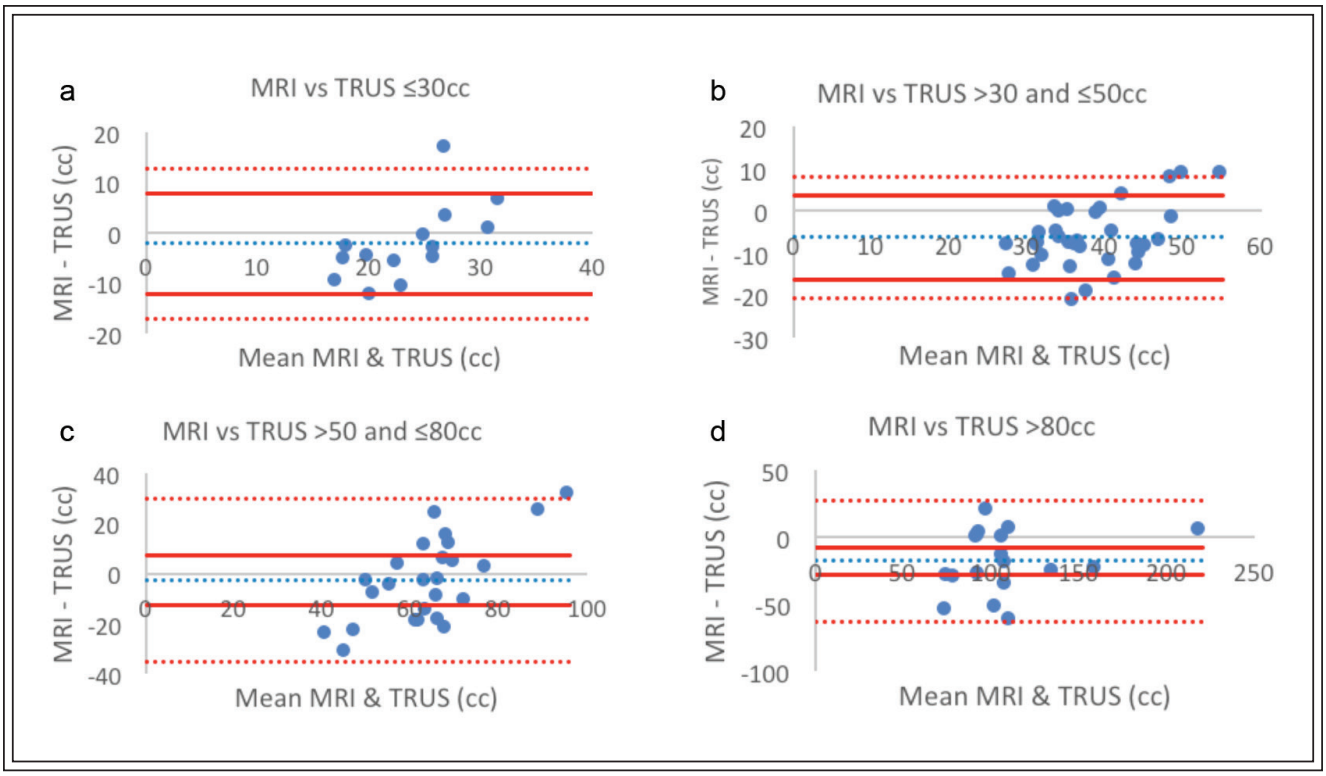

Figure 3. Bland-Altman analysis comparing average volume as recorded by TRUS and MRI to the difference between volume measurements stratified by volume as recorded by TRUS with clinical LOA of ± 10cc.

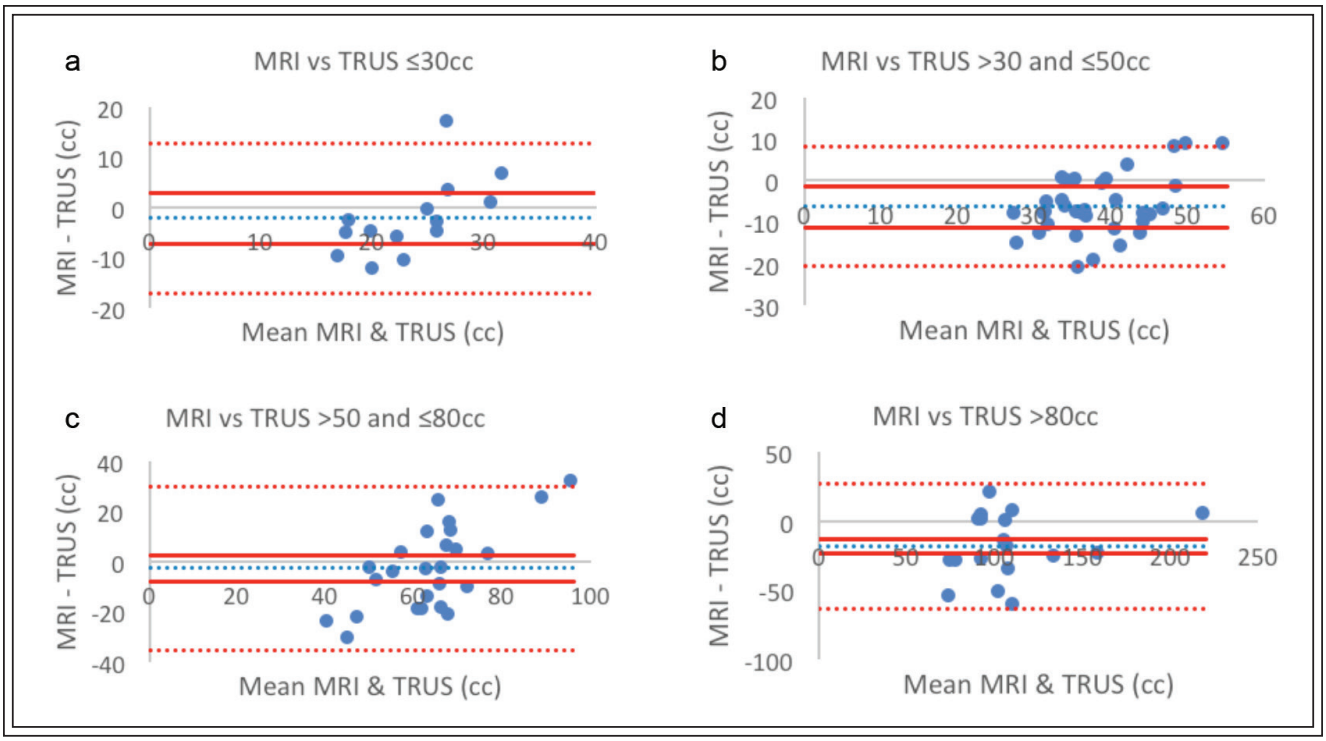

Figure 4. Bland-Altman analysis comparing average volume as recorded by TRUS and MRI to the difference between volume measurements stratified by volume as recorded by TRUS with clinical LOA of ± 5cc.

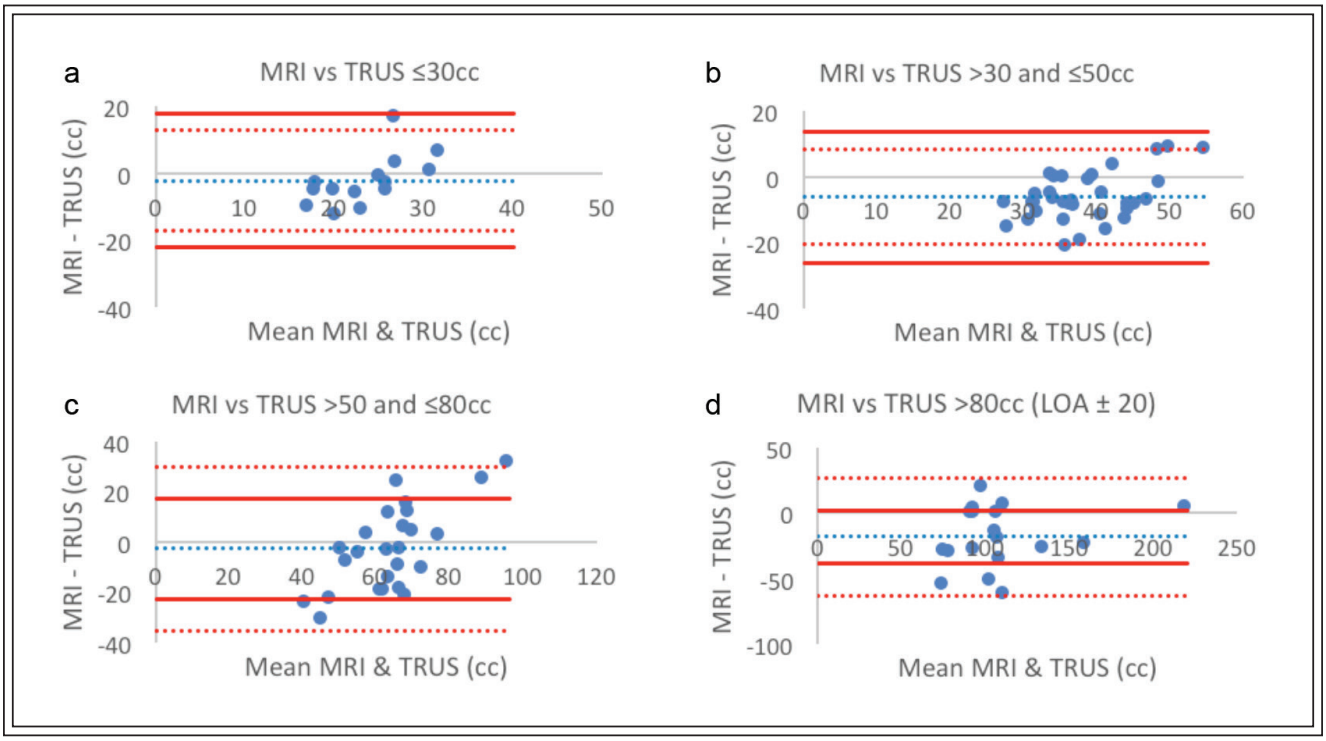

Figure 5. Bland-Altman analysis comparing average volume as recorded by TRUS and MRI to the difference between volume measurements stratified by volume as recorded by TRUS with clinical LOA of ± 20cc.

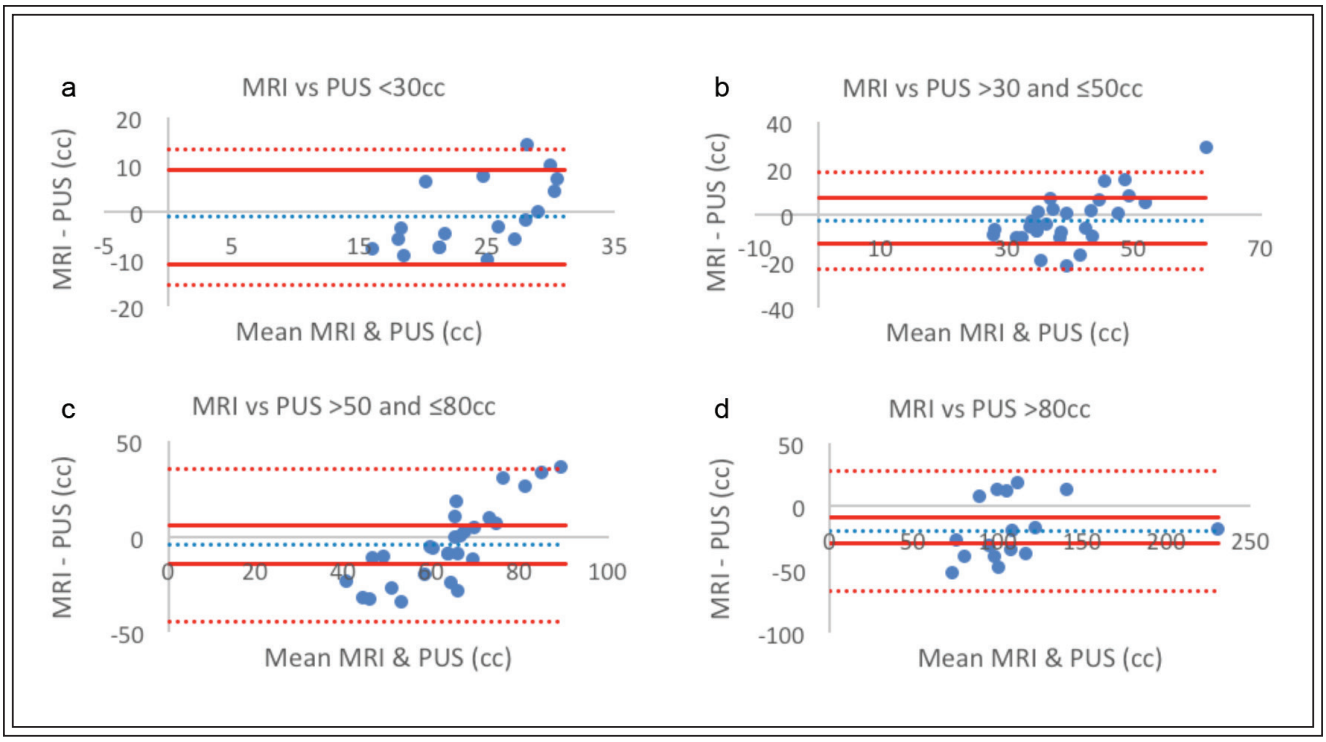

Figure 6. Bland-Altman analysis comparing average volume as recorded by PUS and MRI to the difference between volume measurements stratified by volume as recorded by PUS with clinical LOA of ± 10cc.

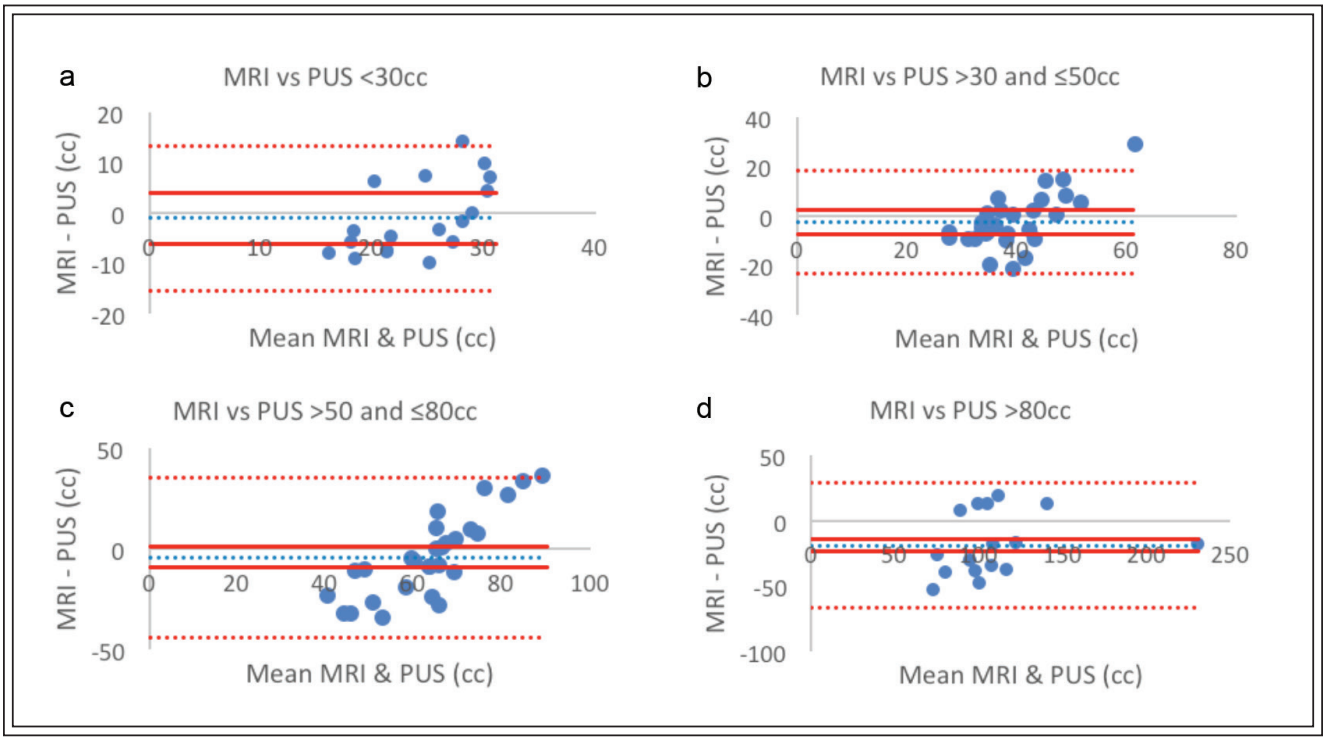

Figure 7. Bland-Altman analysis comparing average volume as recorded by PUS and MRI to the difference between volume measurements stratified by volume as recorded by PUS with clinical LOA of ± 5cc.

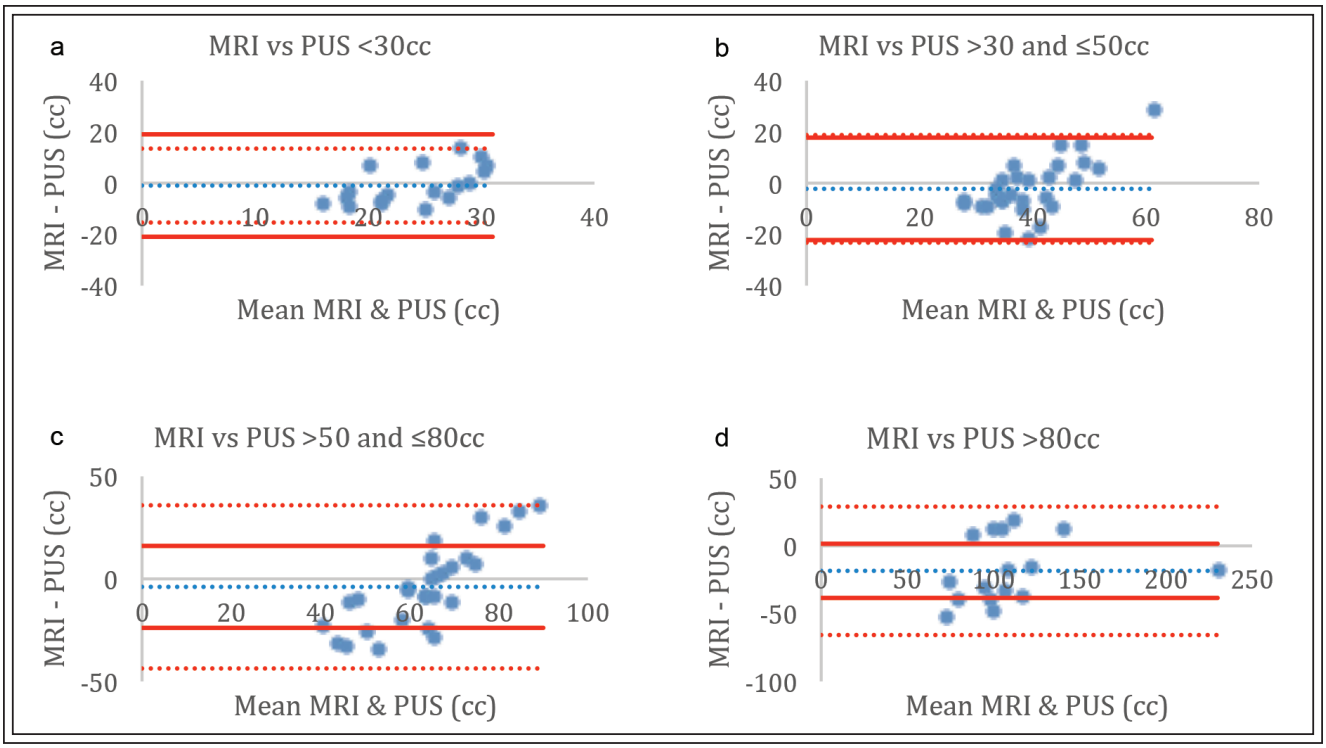

Figure 8. Bland-Altman analysis comparing average volume as recorded by PUS and MRI to the difference between volume measurements stratified by volume as recorded by PUS with clinical LOA of ± 20cc.

all three modalities, as well as for MRI versus TRUS. There was good reliability between MRI and PUS (ICC of 0.50-0.75 = moderate reliability, 0.75-0.9 = good reliability, > 0.90 = excellent reliability).[22] When data was stratified by patient BMI (subgroups ≤ 25, > 25 to ≤ 30, and > 30 kg/m^2) ICC values were good to excellent for all comparisons. Stratifying data by time between exams revealed that the reliability was moderate for patients who received TRUS and MRI 3 to 4 years apart and patients who received PUS and MRI 1 to 2 years apart. All other comparisons remained good to excellent. Notably, ICC values for imaging taken greater than 1 year apart had wide confidence intervals, likely due to the low number of patients in these groups.

Several studies have compared TRUS to MRI in estimating prostate size. Dianat et al calculated ICC for MRI versus TRUS as 0.93 (95% CI 0.87-0.96), which is consistent with our own findings.[21] Others have demonstrated good to excellent reliability when comparing TRUS and MRI to surgical specimen weight.[9,21] To our knowledge, ours is the first study to calculate the ICC to determine reliability for PUS compared to MRI, as well as PUS, TRUS, and MRI together in estimating prostate size.

In addition to evaluating correlation, we used BA analysis to determine agreement. We prefer clinical LOA set at ± 10 cc to reflect a clinically acceptable range of prostate volumes that would not be likely to change diagnostic or therapeutic decisions. We do understand that different practitioners may have different thresholds for this acceptable range, and thus included data for clinical LOA of ± 5 cc and ± 20 cc as well. For both PUS and TRUS compared to MRI, ≥ 79% of data fell within our clinically acceptable limits of ± 10 cc for prostates ≤ 30 cc and > 30 cc to ≤ 50cc. This suggests that PUS and TRUS may be used interchangeably with MRI to measure prostates of this size. Conversely, for prostates > 50 cc to ≤ 80 cc and > 80 cc, PUS and TRUS compared to MRI resulted in ≤ 46% of data within our clinically acceptable limits of ± 10 cc. This suggests that for larger prostates > 50 cc, PUS and TRUS are not interchangeable with MRI.

For those with a more stringent approach as to an acceptable prostate volume measurement, clinical LOA of ± 5 cc are used. Using this smaller range, the highest proportion of values falling within these limits is only 57% for MRI versus TRUS in prostates ≤ 30 cc and 44% for MRI versus PUS in prostates > 30 to ≤ 50 cc. Based on this smaller range set by the clinical LOA of ± 5, the data suggests neither TRUS nor PUS would be interchangeable with MRI at any prostate volume.

For those who with a more flexible approach as to an acceptable prostate volume measurement, clinical LOA of ± 20 cc are used. Using this larger range, 100% of values fall within the clinical LOA in prostates ≤ 50 cc in volume, and 80% of values fall within the clinical LOA in prostates > 50 to ≤ 80 cc, though only 61% of values fall within the larger clinical LOA for prostates > 80 cc. These data suggest that in prostates ≤ 80 cc TRUS may be used interchangeably with MRI to measure prostate volume, as opposed to only in prostates ≤ 50 cc when using clinical LOA of ± 10 cc. When using this larger range for clinical LOA of ± 20 to compare PUS to MRI, 100% of the data falls within the clinical LOA for prostates ≤ 30 cc and 97% for prostates > 30 cc to ≤ 50 cc. Only 64% and 44% of the data falls within these clinical LOA in prostates > 50 to ≤ 80 cc, and > 80 cc, respectively. Using clinical LOA of ± 20 cc thus suggests that PUS may be used interchangeably with MRI in sizing of prostates smaller than 50 cc, the same result as was achieved using clinical LOA of ± 10 cc.

Our results may be compared with two prior studies that used BA analysis to compare TRUS to MRI.[9,21] Both Martins et al and Dianat et al interpreted their BA analysis as demonstrating good agreement between these two imaging modalities. Notably, neither of these studies stratified prostates by volume or included evaluator-determined limits of agreement, as is done in our analysis. Ours is the first study to our knowledge to evaluate agreement between PUS and MRI using BA analysis.

This study has several limitations. The method by which prostate volume is calculated is one such limitation. We chose to use the ellipsoid formula in calculating prostate volume, though this is only one of several available formulas used in calculating prostate volume. Notably, Terris compared 15 different methods of volume estimation using measurements from TRUS, which were compared to specimen weights.[23] They found that the optimal formula for calculating estimated volume differed depending on whether prostates were greater or less than 80 grams. Additionally, several studies have highlighted the consequences of inconsistencies among prostate volume calculation methods. Murciano-Goroff et al studied patients under consideration for brachytherapy whose prostate volume was estimated by contoured axial ultrasound slices, ultrasound ellipsoid calculation, and endorectal coil MRI ellipsoid calculation.[24] They found that a full 33.3% of those who qualified for brachytherapy based on ellipsoid ultrasound volume would have been disqualified by one or both of the other two modalities. These results suggest that prostates do not grow uniformly at all sizes and demonstrate potential consequences of variation between different sizing methods. We were unable to evaluate the accuracy of various formulas to estimate prostate size in our study because not all necessary dimensions were available in our medical records.

Time between US and MRI exams varied among patients in our study from 8 days to 4 years. Though patients with interim procedures that could have impacted prostate size were excluded from the study, it is possible that prostate growth between exams impacted the differences between measurements. Due to the relatively slow annual growth rate of the prostate, estimated at 1.6% per year, we feel this is unlikely to have impacted study results.[25] Though analysis of ICC for patients with more than 1 year between exams was limited by large confidence intervals, values were not dramatically different from those who received imaging within 1 year. BA analysis of data limited to patients with imaging within 1 year was performed and did not alter our conclusions, thus we chose to include patients with imaging up to 4 years apart.

This study does not account for the effect of a median lobe on estimation of prostate volume. Documentation of whether or not a median lobe was present was only done in a minority of cases (19%). Unfortunately, the remainder of cases did not specify in the reports whether or not median lobe was present. Data about the median lobe was gathered from documentation in surgeons' clinic notes and whether or not this was recorded was not consistent amongst patients. In addition, we were unable to control for bladder volume during PUS. Intravesical protrusion of the prostate increases with decreasing bladder size, and PUS measurements have been shown to correlate best with TRUS at bladder volumes less than 400 milliliters.[26] It is routine practice at our institution to instruct patients to come to the clinic with a full bladder, however actual bladder volume is a potentially confounding variable based on the degree of intravesical prostatic protrusion.

It is possible that there was both inter-operator variability and variability within a single operator in ultrasound measurements. In their 1996 study, Bazinet et al found that on average there was 25% variability between two consecutive measurements of the prostate for the same prostate when measured by one of five attending urologists who had performed 5,000 cumulative evaluations.[27] Though the vast majority of ultrasounds were performed by our dedicated ultrasonographer, a small percentage of PUS were recorded by attending urologists. Our analysis would

be strengthened by the use of a single operator, though due to the small portion of measurements recorded by attending urologists, inter-operator variability would be unlikely to significantly alter our findings. Our dedicated and certified ultrasonographer has performed over 10,000 each of PUS and TRUS over 40 years. Furthermore, the improvements in ultrasound technology over the last few decades have likely reduced the variability of prostate measurements and calculated volumes.[28-31] We acknowledge the potential for single operator variability, though we feel the experience of our ultrasonographer and advancements in technology likely minimized this effect.

As with ultrasound, there is the potential for variability between measurements with MRI, however our institution is fortunate to have a dedicated radiologist who evaluated prostate images during the study period. This removes potential inter-operator variation, however there is still a possibility of variation within that operator's own readings. Due to the use of a single, experienced radiologist, we feel the potential for variability between readings is unlikely to significantly impact our results.

A notable aspect of this study is the decision to set clinical LOA for BA analysis at ± 10 cc. As described above, these limits reflect the level of variation in measurements obtained by different imaging modalities that providers at our institution thought was reasonable. It is important in interpreting our results to consider one's own comfort with prostate volume measurement, and what would be considered a large enough difference in estimated volume to change diagnostic or therapeutic decision-making.

Future studies could benefit from accounting for the limitations that we mention above. As it has been suggested that optimal formula for prostate volume depends on size, one could compare interchangeability between ultrasound and MRI for different estimation formulas. In addition to the formula itself, the potential impact of median lobe on prostate volume estimation warrants further investigation. Future research should assess how median lobe characteristics impact the accuracy of these formulas. As we show PUS to be interchangeable with MRI at smaller prostate volumes, this comparably inexpensive, quick, and less invasive exam has the potential to impact patient satisfaction and hospital costs, both of which could be examined in future research.

MRI is the gold standard imaging modality for prostate cancer diagnosis and pre-treatment planning including volumetric analysis and although it is increasingly available, it remains a time-intensive and expensive test. Ultrasound is rapid, readily available and inexpensive and should be the initial imaging modality to size the prostate, especially in the outpatient clinic. In smaller prostates < 50 cc, one may consider size estimates based on ultrasound to be interchangeable with those based on MRI. However, for larger prostates in settings where size may alter management, cross-sectional imaging should be considered.

Conclusions

MRI is interchangeable with TRUS and PUS for prostate sizing at prostate volumes ≤ 50 cc. However, for larger prostates in settings where size may alter surgical management, cross-sectional imaging may be warranted. □

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