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# Indications for additional volume studies for gland volume estimation in prostate cancer brachytherapy

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## ABSTRACT

An estimated gland volume of > 60 cc is a relative contraindication to brachytherapy for prostate cancer. As volume estimation using biopsy ultrasound (Bx-US) alone may be inaccurate, many centers perform additional volume assessments prior to the brachytherapy procedure. At the study institution, computed tomography (CT) based volume assessments were routinely performed on all patients to determine brachytherapy eligibility. This study aimed to determine whether this CT imaging could be omitted for certain Bx-US based gland volume estimates. To investigate this, 1576 consecutive patients that received ultrasound based intraoperatively planned brachytherapy at a single comprehensive cancer center between 2003 and 2021 were reviewed. Gland volume as estimated by Bx-US, CT and magnetic resonance (MR) imaging were compared to intraoperatively contoured gland volume (ICGV) or the larger contoured gland volume on CT for any patients receiving neo-adjuvant androgen deprivation therapy (ADT) for gland downsizing (IM-US-corr). There was a significant difference between IM-US-corr and estimated gland volume for Bx-US ($P < 0.001$) and MR ($P < 0.001$), but not CT ($P = 0.160$). Bx-US and MR tended to underrepresent the IM-US-corr, with a > 20% difference from actual volume in 31% and 59% of cases, respectively. When Bx-US volume was estimated to be < 40 cc, < 50 cc and < 60 cc, an IM-US-corr > 60 cc was encountered in 2%, 5% and 7% of cases, respectively. In contrast, IM-US-corr > 60 cc was encountered in 0.2%, 1% and 2% of cases for CT estimates of < 40 cc, < 50 cc and < 60 cc. In patients with an estimated gland volume of < 50 cc by Bx-US, dedicated pre-operative volume studies are unlikely to alter management. However, patients above this cut-off stand to benefit from the use of additional volume assessment to better delineate gland volume and determine eligibility for brachytherapy.

**Keywords:** Prostate brachytherapy; prostate gland volume estimation; brachytherapy planning; prostate size

## INTRODUCTION

Prostate cancer is among the most commonly diagnosed malignant neoplasms in North America. [1–3] Although survival outcomes are excellent compared to most cancers, both disease- and treatment-related morbidity can adversely impact quality of life. Brachytherapy is a commonly recommended treatment modality due to its proven efficacy and low-toxicity profile. However, its use is sometimes limited in patients with an estimated gland volume of > 60 cc which has traditionally been considered to be a relative contraindication due to an increased risk of public arch interference or risks the prostate dimensions exceed those of the implantation template [4–6]. In these cases, most clinicians recommend the use of androgen deprivation therapy (ADT) for gland volume reduction prior to brachytherapy or use of an alternate treatment modality.

The decision of whether brachytherapy may be technically feasible based on gland size, is complicated by the fact that the estimated gland size determined by ellipsoid formula and ultrasound based measurements at the time of biopsy may differ greatly from the true gland size as contoured at the time of seed implantation (this may in turn be due to inaccurate prostate width or height measurements related to pressure from the tans-rectal ultrasound probe or presence of a median lobe). While the use of additional volume studies may assist in more accurately estimating gland size, it is not well-defined as to which patients stand to benefit from additional imaging or what the accuracy of different imaging modalities is for this purpose. This study compared the rate of concordance between biopsy ultrasound (Bx-US), computed tomography (CT), magnetic resonance imaging (MR) and the contoured gland volume on implant ultrasound (ICGV) or a corrected

gland volume which used CT contoured volume in patients receiving ADT for gland downsizing (IM-US-corr) for ICGVs < 60 cc. The main objective was to define the patient population that would most benefit from additional volume studies and identify which imaging modality was ideal for this purpose.

## MATERIALS AND METHODS

This study analyzed 1576 patients receiving either intraoperatively planned low-dose-rate or high-dose-rate brachytherapy as part of definitive management for prostate cancer between 2003 and 2021 at a single academic institution and quaternary cancer center. All patients were referred to a radiation oncologist after having a 12 core biopsy come back positive for prostate adenocarcinoma. At the time of needle core biopsy, standard procedures included volume measurement of the prostate. The superior/inferior, anterior/posterior and lateral dimensions were standardly used to estimate prostate volume using the ellipsoid formula [$V = \pi/6$ abc] and included in synoptic reporting. Pathology was centrally reviewed by dedicated genitourinary pathologists. In patients receiving 3-Tesla MR imaging as part of their initial staging workup, a similar estimate of prostate volume using the same dimensions and formula was routinely included as part of synoptic reporting by body radiologists with dedicated genitourinary experience.

Patients were routinely recommended to undergo brachytherapy monotherapy for NCCN low risk disease (if refusing active surveillance) or NCCN favorable intermediate risk disease. Otherwise, patients were to have recommended brachytherapy boost routinely for unfavorable intermediate or high risk disease. For unfavorable or high risk disease, patients were routinely recommended at least 3 months of neo-adjuvant ADT [7]. Practice patterns were considerably different between practitioners but in general for gland volumes > 100 cc on Bx-US, brachytherapy was discouraged irrespective of ADT use.

Patients consenting to treatment then went on to receive a routine CT based prostate volume assessment as part of standard pre-brachytherapy workup. There was no mechanism for pre-brachytherapy ultrasound-based volume assessments in the dorsal lithotomy position at the study center over the study period. For patients receiving ADT as part of their management plan, this was routinely within the first month of androgen deprivation (ADT). The prostate was then contoured on these image sets and the volume was used to determine whether neo-adjuvant ADT should be used or whether brachytherapy would not be recommended. For contoured prostate gland volumes larger than 60 cc, ADT therapy was routinely recommended and a subsequent CT scan was used after 2–3 months to ensure an adequate reduction in prostate gland volume was obtained. Finally, at the time of implantation, the prostate gland was routinely contoured as the clinical target volume for planning purposes.

As part of an ongoing quality improvement process aimed at streamlining brachytherapy processes at the host institution a complete revision of the established prostate brachytherapy procedures and processes was undertaken in 2021. This identified potential excessive use of resources and inconvenience to patients from the routine practice of performing a CT based volume assessment prior to brachytherapy. The authorship aimed to determine if an easily interpretable set of criteria could be created to identify which patients should proceed with

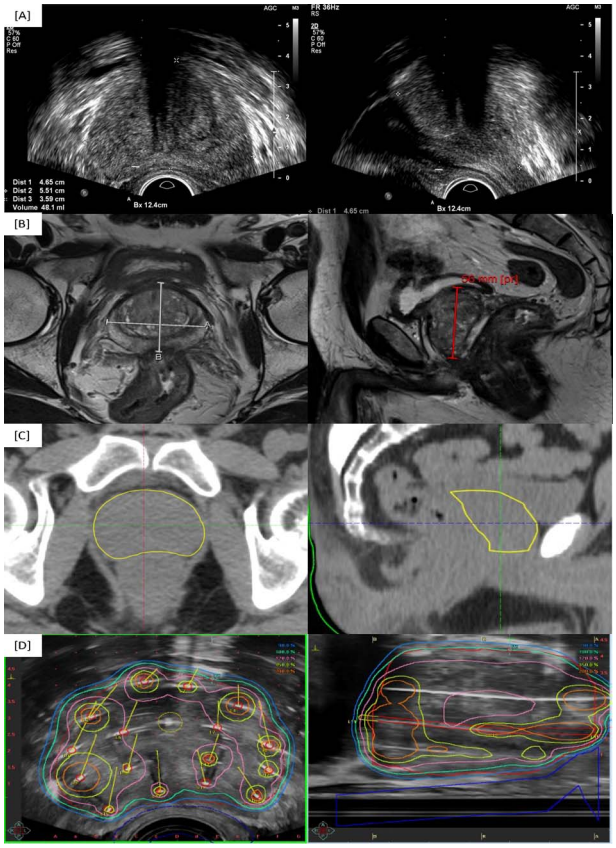


**Fig. 1. Example of typical volume assessments at the time of (A) trans-rectal ultrasound guided biopsy (width, height and length measurement), (B) MR imaging (width, height and length measurement), (C) CT based volume assessment (yellow contoured volume) and (D) the time of brachytherapy (red volume contour).**

volume assessments. To accomplish this, the electronic medical record was explored and all reported volumes were extracted from Bx-US and MR synoptic reporting. Additionally, whether the patient received ADT prior to brachytherapy was recorded. Then the CT volume assessment and ICGV were extracted from the local treatment planning systems (Fig. 1 shows an example of how volumes were assessed across modalities).

Descriptive statistics including median (inter-quartile-range)[range] and count data with proportions were used to describe the data. To account for changes in gland volume from ADT and potential risk of underestimating the gland volume cut-offs necessary, an exploratory variable IM-US-corr was created. This was the ICGV for patients not receiving neo-adjuvant ADT or the prostate volume at the time of first CT based volume assessment (CT1) in patients receiving ADT if the ICGV was < 60 cc. Comparisons between each imaging modality's estimates of gland volume were made using the Mann–Whitney–Wilcoxon test and proportions of patients with disagreements greater than 5%, 10%, 20% or 5 cc, 10 cc, 15 cc and 20 cc between modalities were calculated. Then absolute count data was made for each imaging

modality to determine a reasonable cut-off for which patients should undergo volume assessment.

This analysis was conducted as part of a continuous brachytherapy quality improvement process, and was considered minimal risk and as such has a waiver of formal board review by the Health Research Ethics Board of Alberta. Data are only housed on institutional servers as per regional legislation.

## RESULTS AND DISCUSSION

IM-US-corr volume among the patient cohort was 35.7 (29.0–44.4)cc. Estimated gland volume by Bx-US, CT1 and MR were 34.0 (27.0–44.0)cc, 36.9 (30.0–46.0)cc and 30.0 (20.0–42.5)cc, respectively (Table 1). Estimated gland volume by Bx-US ($P < 0.001$) and MR ($P < 0.001$) differed significantly from IM-US-corr, and both methods tended to underestimate IM-US-corr. In contrast, estimated volumes by the minimum volume as contoured on any CT image set ($CT_{min}$) were similar to IM-US-corr ($P = 0.160$), and tended towards being an overestimation of IM-US-corr.

Bx-US gland volume estimation differed from IM-US-corr by > 10% in 445/1055 (42%) patients and by > 20% in 322/1055 (31%) patients. MR gland volume estimation differed from true gland volume by > 10% in 140/210 (67%) patients and by > 20% in 123/210 (59%) patients. $CT_{min}$ gland volume estimation differed from IM-US-corr by > 10% in 106/1016 (10%) patients and by > 20% in 70/1016 (7%) patients.

In patients with a Bx-US estimated volume < 40 cc, the IM-US-corr volume was found to be > 60 cc in 16/1055 (2%) of cases (Table 2). In contrast, using a cut-off of < 50 cc and < 60 cc, 50/1055 (5%) and 75/1055 (7%) of patients had volumes > 60 cc on IM-US-corr, respectively. Among patients with a first CT estimated volume < 50 cc, only 9/1016 (1%) had volumes > 60 cc on IM-US-corr. Rates of IM-US-corr > 60 cc were similarly low for patients that were < 50 cc (9/1016, 1%) and < 60 cc (22/1016, 2%) on CT1. When comparing MR volume thresholds to IM-US-corr volumes, > 60 cc prostate volumes on IM-US-corr were found in 20/210 (10%), 31/210 (15%) and 51/210 (24%) patients that had MR volumes of < 40 cc, < 50 cc and < 60 cc, respectively.

In addition the 896 patients not receiving neo-adjuvant ADT for any reason (including deliberate gland downsizing) were analyzed separately. In these patients, ICGV was 34.4 (29.0–41.1)cc. Estimated gland volume by Bx-US, MR and CT1 were 31.6 (26.0–40.0)cc, 31.8 (22.3–42.9)cc and 35.2 (29.5–43.0)cc, respectively. When comparing Bx-US imaging thresholds to ICGV, > 60 cc volumes were found in 8/896 (1%), 26/896 (3%) and 31/896 (3%) patients that had Bx-US volumes of < 40 cc, < 50 cc and < 60 cc, respectively (Table 3). When comparing MR imaging thresholds to ICGV, > 60 cc volumes were found in 8/156 (5%), 15/156 (10%) and 24/156 (15%) patients that had MR volumes of < 40 cc, < 50 cc and < 60 cc, respectively.

This quality improvement process investigated the rate of gland volume estimation in a cohort of 1576 patients that underwent brachytherapy to delineate a cut-off for additional volume assessments beyond the Bx-US estimated gland volume. Patients with > 50 cc Bx-US-estimated gland volume were found to have a likely < 5% probability of encountering a contoured gland volume of > 60 cc at the time of brachytherapy (based on IM-US-corr and assuming

**Table 1. Comparison of volume assessments across modalities, values are given as median (inter-quartile-range) [range] or absolute count (%) as appropriate**

| Variable 1 | Variable 2 | MWW *P*-value | # Cases > 5% off** | # Cases > 10% off | # Cases > 20% off | # Cases > 5 cc off | # Cases > 10 cc off | # Cases > 15 cc off | # Cases > 20 cc off |
|---|---|---|---|---|---|---|---|---|---|
| **Bx-US** | **ICGV** | | *n* = 1284 | | | | | | |
| 34.0 (27.0–44.0) [0–97.8] | 34.8 (28.9–42.0) [6.7–143.9] | 0.282 | 583 (45%) | 498 (39%) | 357 (28%) | 388 (30%) | 188 (15%) | 89 (7%) | 44 (3%) |
| **Bx-US** | **CT1** | | *n* = 1228 | | | | | | |
| 34.0 (27.0–44.0) [0–97.8] | 36.9 (30.0–46.0) [14.6–109.8] | < 0.001 | 664 (54%) | 572 (47%) | 388 (32%) | 505 (41%) | 275 (22%) | 139 (11%) | 74 (6%) |
| **CTmin** | **ICGV** | | *n* = 1178 | | | | | | |
| 36.9 (30.0–45.6) [14.6–109.8] | 34.8 (28.9–42.0) [6.7–143.9] | < 0.001 | 190 (16%) | 149 (13%) | 98 (8%) | 119 (10%) | 50 (4%) | 22 (2%) | 13 (1%) |
| **MR** | **ICGV** | | *n* = 372 | | | | | | |
| 30.0 (20.0–42.5) [0.0–96.7] | 34.8 (28.9–42.0) [6.7–143.9] | < 0.001 | 245 (66%) | 227 (61%) | 194 (52%) | 212 (57%) | 152 (41%) | 106 (28%) | 83 (22%) |
| **MR** | **CT1** | | *n* = 318 | | | | | | |
| 30.0 (20.0–42.5) [0.0–96.7] | 36.9 (30.0–46.0) [14.6–109.8] | < 0.001 | 217 (68%) | 194 (61%) | 163 (51%) | 182 (57%) | 122 (38%) | 94 (30%) | 72 (23%) |
| **Bx-US** | **IM-US-corr*** | | *n* = 1055 | | | | | | |
| 34.0 (27.0–44.0) [0–97.8] | 35.7 (29.0–44.4) [12.8–143.9] | < 0.001 | 512 (49%) | 445 (42%) | 322 (31%) | 368 (35%) | 188 (18%) | 102 (10%) | 61 (6%) |
| **CTmin** | **IM-US-corr*** | | *n* = 1016 | | | | | | |
| 36.9 (30.0–45.6) [14.6–109.8] | 35.7 (29.0–44.4) [12.8–143.9] | 0.160 | 121 (12%) | 106 (10%) | 70 (7%) | 92 (9%) | 53 (5%) | 30 (3%) | 19 (2%) |
| **MR** | **IM-US-corr*** | | *n* = 210 | | | | | | |
| 30.0 (20.0–42.5) [0.0–96.7] | 35.7 (29.0–44.4) [12.8–143.9] | < 0.001 | 154 (73%) | 140 (67%) | 123 (59%) | 133 (63%) | 98 (47%) | 75 (36%) | 57 (27%) |

*For IM-US-corr, cases where HT was used and the volume at the time of implant was < 60 cc, the implant gland volume was substituted for the CT1 gland volume) ** calculated as number of cases (% of those with data available) where variable 2 is X% greater or Xcc greater than variable 1.

**Table 2. Number (%) of brachytherapy cases with discordance in gland volume assessment among different imaging modalities. Values are given as absolute count/total available cases (%)**

| | **Bx-US > 60 cc** | **CT1 > 60 cc** | **MR > 60 cc** | **ICGV > 60 cc** | **IM-US-corr > 60 cc** |
|---|---|---|---|---|---|
| **Bx-US < 40 cc** | | 8/1228 (1%) | 2/396 (0.5%) | 10/1284 (1%) | 16/1055 (2%) |
| **Bx-US < 50 cc** | | 32/1228 (3%) | 5/396 (1%) | 30/1284 (2%) | 50/1055 (5%) |
| **Bx-US < 60 cc** | | 55/1228 (5%) | 12/396 (3%) | 37/1284 (3%) | 75/1055 (7%) |
| **CT1 < 40 cc** | 15/1228 (1%) | | 0/318 (0%) | 2/1178 (0.2%) | 2/1016 (0.2%) |
| **CT1 < 50 cc** | 37/1228 (3%) | | 4/318 (1%) | 9/1178 (1%) | 9/1016 (1%) |
| **CT1 < 60 cc** | 48/1228 (4%) | | 8/318 (3%) | 22/1178 (2%) | 22/1016 (2%) |
| **MR < 40 cc** | 6/396 (2%) | 13/318 (4%) | | 10/372 (3%) | 20/210 (10%) |
| **MR < 50 cc** | 9/396 (2%) | 17/318 (5%) | | 19/372 (5%) | 31/210 (15%) |
| **MR < 60 cc** | 11/396 (3%) | 29/318 (9%) | | 32/372 (9%) | 51/210 (24%) |
| **ICGV < 40 cc** | 18/1284 (1%) | 21/1178 (2%) | 4/372 (1%) | | 18/1155 (2%) |
| **ICGV < 50 cc** | 51/1284 (4%) | 47/1178 (4%) | 10/372 (3%) | | 42/1155 (4%) |
| **ICGV < 60 cc** | 70/1284 (5%) | 69/1178 (6%) | 18/372 (5%) | | 62/1155 (5%) |
| **IM-US-corr < 40 cc** | 13/1055 (1%) | 0/1016 (0%) | 0/210 (0%) | 0/1155 (0%) | |
| **IM-US-corr < 50 cc** | 34/1055 (3%) | 0/1016 (0%) | 3/210 (1%) | 0/1155 (0%) | |
| **IM-US-corr < 60 cc** | 41/1055 (4%) | 1/1016 (0.1%) | 6/210 (3%) | 0/1155 (0%) | |

*For IM-US-corr, cases where HT was used and the volume at the time of implant was < 60 cc, the implant gland volume was substituted for the CT1 gland volume)

**Table 3. Number (%) of brachytherapy cases with discordance in gland volume assessment among different imaging modalities for all patients not receiving hormone therapy. Values are given as absolute count/total available cases (%)**

| | **Bx-US > 60 cc** | **CT1 > 60 cc** | **MR > 60 cc** | **ICGV > 60 cc** |
|---|---|---|---|---|
| **Bx-US < 40 cc** | | 2/849 (0%) | 0/166 (0%) | 8/896 (1%) |
| **Bx-US < 50 cc** | | 10/849 (1%) | 1/166 (1%) | 26/896 (3%) |
| **Bx-US < 60 cc** | | 11/849 (1%) | 3/166 (2%) | 31/896 (3%) |
| **CT1 < 40 cc** | 8/849 (1%) | | 0/128 (0%) | 2/821 (0%) |
| **CT1 < 50 cc** | 14/849 (2%) | | 0/128 (0%) | 9/821 (1%) |
| **CT1 < 60 cc** | 14/849 (2%) | | 1/128 (1%) | 18/821 (2%) |
| **MR < 40 cc** | 0/166 (0%) | 2/128 (2%) | | 8/156 (5%) |
| **MR < 50 cc** | 0/166 (0%) | 3/128 (2%) | | 15/156 (10%) |
| **MR < 60 cc** | 0/166 (0%) | 6/128 (5%) | | 24/156 (15%) |
| **ICGV < 40 cc** | 8/896 (1%) | 3/821 (0%) | 0/156 (0%) | |
| **ICGV < 50 cc** | 16/896 (2%) | 5/821 (1%) | 1/156 (1%) | |
| **ICGV < 60 cc** | 16/896 (2%) | 6/821 (1%) | 2/156 (1%) | |

there would be no ADT used). If one assumes an encounter rate of 5% of patients having an unconfirmed large prostate at the time of brachytherapy, this should have a very low impact on brachytherapy operating room workflows and a much lower rate of having to abandon a case due to technical challenges. At the study center, this rationale was used to set a cut-off of 50 cc on Bx-US to determine which patients should proceed to have additional volume studies when planning for high-dose-rate brachytherapy.

As the incidence of prostate cancer is projected to rise in North America, prudent resource stewardship and clinical decision-making tools will be vital in guiding patient management. The use of additional volume studies in all cases had the potential to expose patients to unnecessary radiation from CT and put a burden on health resources. Additionally, due to the difficulty of accessing CT and MR imaging in single-payer healthcare systems, unnecessary volume studies may delay patient treatment and adversely affect disease-related outcomes [8].

This study was subject to all of the limitations of a retrospective analysis. Additionally, this study could not account for pubic arch interference encountered due to narrow pelvic boney anatomy. In individuals with small body size, even a gland < 60 cc may possibly be at risk of pubic arch interference. Additionally, when varying seed activity or source selection based on volume, additional volume studies may still be required to determine the inferior cut-off in patients with excessively small prostate glands. Due to the single-center design of this study, it is unknown whether the cut-offs identified here are generalizable to other centers with different treatment and supportive care practices or expertise. Of particular note, this study may not be applicable

when considering low-dose-rate prostate brachytherapy techniques as in many centers, seed ordering is dependent on prostate gland volume. However, the data should be easily transferable to centers that utilize a dedicated ultrasound based volume assessment in the dorsal lithotomy position for high-dose-rate brachytherapy.

In summary, this project found that patients with < 50 cc estimated gland volume on Bx-US are unlikely to benefit from additional volume studies unless required for determining seed activity or number of seeds. Patients with > 50 cc estimated gland volume on Bx-US should receive dedicated prostate volume assessments.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## REFERENCES

1. Siegel RL, Miller KD, Fuchs HE et al. Cancer statistics-2021. *CA Cancer J Clin* 2021;71:7–33.
2. Quon H, Loblaw A, Nam R. Dramatic increase in prostate cancer cases by 2021. *BJU Int* 2011;108:1734–8.
3. Brenner DR, Weir HK, Demers AA et al. Projected estimates of cancer in Canada in 2020. *Can Med Assoc J* 2020;192:E199–205.
4. Hoskin PJ, Colombo A, Henry A et al. GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: an update. *Radiother Oncol* 2013;107:325–32.
5. Yamada Y, Rogers L, Demanes DJ et al. American Brachytherapy Society consensus guidelines for high-dose-rate prostate brachytherapy. *Brachytherapy* 2012;11:20–32.
6. Prestidge BR, Prete JJ, Buchholz TA et al. A survey of current clinical practice of permanent prostate brachytherapy in the United States. *Int J Radiat Oncol Biol Phys* 1998;40:461–5.
7. D'Amico AV, Chen M-H, Renshaw A et al. Long-term follow-up of a randomized trial of radiation with or without androgen deprivation therapy for localized prostate cancer. *JAMA* 2016;314:1291–3.
8. Khanolkar RA, Quon H, Thind K et al. Excessive waitlists and delays to treatment with low-dose-rate brachytherapy predict an increased risk of recurrence and metastases in intermediate-risk prostatic carcinoma. *Clin Transl Radiat Oncol* 2021;30:38–42.