A Simple Technique for Calculation of the Volume of Prostatic Adenocarcinomas in Radical Prostatectomy Specimens

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Summary

Tumor volume has been suggested as an important prognostic factor of prostatic adenocarcinoma (PAC) treated with radical prostatectomy (RP). The calculation of tumor volume is complicated by the difficulty in appreciation of tumor nodules at gross examination, multifocality, and variation in the shape of tumor nodules. We propose a simple technique for the calculation of tumor volume.

One hundred consecutive specimens of RP were studied with special attention to the shape of tumor nodules. Most small PAC, transitional zone (TZ) PAC, peripheral zone (PZ) PAC without associated benign prostatic hyperplasia (BPH), and PZPAC with Gleason’s score (GS) > 3 + 4 had an ovoid shape. Most large sized nodules of PZPAC with GS < 4 + 3 tended to mold according to the boundaries of the TZ that were themselves often compressed by hyperplastic nodules. Therefore, these large tumor nodules were crescentically shaped and had tapering pole(s). We deduced from this tendency that the ratio of height of the tumor nodule = D₁ × the height/greatest horizontal diameter of the prostate (D₃₁ = the greatest diameters of the largest section of tumor nodule). Using the mathematical formula for volume of an ellipsoid structure, we propose the following formula to calculate the volume of each tumor nodule = 0.8 × K × D₁ × D₂ (D₂ = greatest diameter orthogonal to D₁, and K = coefficient for correction of tumor volume due to the compression of hyperplastic nodules). K is empirically estimated as 2/3 for PZPAC in mid prostate and 1/2 for tumor nodules at the apex and base. The total tumor volume is the sum of all tumor nodule volumes.

By measuring the two greatest orthogonal diameters, D₁ and D₂, of the largest horizontal section of a tumor nodule, we were able to calculate the corresponding volume and consequently the total tumor volume of the prostate. Analysis of the calculated total tumor volume showed a good correlation with the current technique of measurement on each section of the prostate, particularly for tumors ranging from 1.5 to 3.0 cm³.

Key words: Prostate – Adenocarcinoma – Volume

Introduction

Important prognostic factors obtained from radical prostatectomy (RP) for patients with prostatic adenocarcinoma (PAC) are tumor Gleason’s score (GS), stage which includes volume, status of tumoral involvement...
of the capsule, extracapsular tissue, seminal vesicles, and regional lymph nodes [3, 5, 7, 8, 10, 11, 13, 14, 23]. Tumor volume has been suggested as a strong predictor of lymph node metastasis [1, 6, 9, 16, 20]. The calculation of tumor volume is complicated by the difficulty in appreciation of tumor nodules at gross examination, multifocality, and variation in the shape of tumor nodules [4]. While the accurate measurement of tumor volume requires meticulous computer-assisted image analysis or grid morphometric work [12, 15, 21], visual estimation is subjective and likely inconsistent [2, 12, 15]. In this study, we examined the distribution and shape of tumor nodules of varying sizes in different prostatic zones in their three dimensional reconstruction, then deduced a common geometric pattern of tumor growth, and applied the mathematical formula to consistently calculate the tumor volume.

Materials and Methods

One hundred consecutive specimens of RP for PAC without preoperative hormonal therapy were received at the surgical pathology Laboratory of the Ottawa Hospital – Civic Campus from December 2000 to December, 2001. All RP specimens were fixed in 40% buffered formaldehyde overnight; we then measured the greatest transverse diameter, antero-posterior diameter and the height of the gland; finally, specimens were serially sectioned into horizontal sections of 0.3 cm thickness. The large sections were divided, if necessary, into two to four blocks of tissue for routine processing. Four micron-thick sections were stained with hematoxylin phloxine saffron stain.

Tumor nodules were categorized into small or large depending on the size smaller or greater than 0.6 cm (small nodule would be identified in no more than one or two consecutive sections- 0.3 or 0.6 cm thickness). Tumor volume was obtained by:

1) Current technique of measurement: by adopting a previously described method [15] with modification in the technique of measuring the surface area of the tumor. The surface of each tumor nodule on each section was calculated by assuming the tumor area as an elliptical shape and by applying the formula: \( S = 3.14 \times R_1 \times R_2 \) in which \( R_1 \) and \( R_2 \) were the greatest orthogonal radii of the area. The volume of the carcinoma was obtained by the product of total tumor surface \( \times \) giant section thickness (0.3 cm) \( \times \) coefficient of fixation retraction (1.5) [4]. The height (or total thickness) of a tumor nodule was obtained by multiplying the number of sections crossing the tumor nodule with 0.3 cm (thickness of the tissue block)

2) Proposed technique of calculation of tumor volume: each tumor nodule was identified by viewing the sections of the serial 3 mm thick section of each nodule. By assuming that tumor nodules are of ovoid shape, we applied the mathematical formula to calculate the tumor volume of an ellipsoid structure and adjust the retraction due to retraction secondary to formalin fixation as follows:

\[ \text{Nodule volume} = 1.5 \times \frac{4}{3} \times \pi \times R_1 \times R_2 \times R_3 \]

\((R_1 \times R_2 \times R_3 \) were orthogonal radii of the largest horizontal section, and \( R_3 \) the radius orthogonal to \( R_1 \) and \( R_2 \)). By replacing \( R_1 \), \( R_2 \) and \( R_3 \) by \( D_1 \), \( D_2 \) and height of the nodule (\( D_1 \), \( D_2 \): orthogonal diameter of the largest section of the tumor nodule), that were equal to \( 2R_1 \), \( 2R_2 \) and \( 2R_3 \) respectively (Fig. 1), we had:

\[ \text{Nodule volume} = 0.8 \times D_1 \times D_2 \times \text{height of the nodule} (A) \]

Statistical analysis was performed by using the “Prism” software program to calculate the coefficient of correlation (\( r^2 \)), p value and to obtain the regression line.

Results

PAC were divided into TZPAC and PZPAC. The latter were subdivided into small versus large tumor nodules (less than 0.6 cm versus more than 0.6 cm diameter), those with or without significant BPH, and those having a GS lower or greater than 3 + 4. They were categorized by the stage of the disease and subdivided according to the location of the largest nodule in the apex, in the mid portion or in the base of the prostate (Table 1). The shape of the tumor nodule depended on the tumor size and GS, and tended to mold according to the boundaries of the prostatic zone in which the tumor was located.
A) Estimation of the height of the tumor nodule

In cross sections of the prostate, the height of the nodule is the most difficult diameter to measure. Since tumor nodules tended to mold to the boundaries of the prostatic zone, $D_1$ and height of the nodule are likely proportional to the height and the greatest horizontal (usually antero-posterior) diameter of the prostate. Therefore, the approximate measurement of $D_3$ can be calculated as:

$$\text{Height of the nodule} = D_1 \times \text{height/antero-posterior diameter of the prostate} \ (B)$$

The height/antero-posterior diameter of the prostate ratio ranged from 0.62–1.27 (0.9.4 ± 1.2). Graph 1 shows the correlation between the measured $D_3$ and calculated $D_3$, $r^2 = 0.83$ and p value < 0.001.

B) Tumor shape

1. **TZPAC**. Tumor nodules usually had an ovoid shape similar to hyperplastic nodules (Fig. 1).

2. **PZPAC**. The tumor nodule varied with size and with the grade of the PAC and of the TZ that changed with the presence and the degree of BPH.
   a) Small tumors of less than 5mm in diameter usually had an ovoid shape
   b) Larger tumor nodules:
      1) Tumor nodule in the anterior horn had an ovoid shape owing to the involvement of the adjacent TZ
      2) PAC with GS > 3 + 4. These high grade carcinomas involved the adjacent region of the TZ in all cases with the tumor nodule > 1.5 cm in this study. Therefore, the tumor nodule had an ovoid shape
      3) PAC with GS < 4 + 3: nodules of BPH usually compressed the PZ mainly at the level of the mid-prostate. In this latter region, large tumors were molded according to the adjacent prostatic capsule or to the boundary of the TZ for tumor nodules near the respective boundaries of the PZ. Thus, the cross section of this type of tumor nodule usually had a crescentic shape with or without tapering lower and upper poles (Fig. 2). The tapering poles represented tumor extension into the adjacent upper and/or lower areas of the PZ.

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**Table 1. Number of cases and shape of largest tumor nodules**

<table>
<thead>
<tr>
<th>Total</th>
<th>Stage</th>
<th>Small nodule (&lt; 0.6 cm)</th>
<th>No BPH</th>
<th>With BPH</th>
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<td></td>
<td></td>
<td></td>
<td>Anterior horn mid</td>
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* crescentic shape without tapering pole in 16 cases, with tapering pole in 22 cases

**TZPAC = transitional zone prostatic adenocarcinoma**

**PZPAC = peripheral zone prostatic adenocarcinoma**

**CZPAC = central zone prostatic adenocarcinoma**

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**Graph 1.** Correlation between the calculated and measured heights, coefficient of correlation $r^2 = 0.83$ and p value < 0.001.
4) Tumor nodules at the apex and base were of ovoid shape because they were located at a distance from the TZ (Fig 3, 4).

3. Central zone (CZ) PAC: Tumor nodule had a shape similar to that at the base of the peripheral zone, i.e., ovoid shape with tapering pole toward the mid portion.

C) Calculation of volume of tumor nodule

For tumor nodules with crescentic shape without tapering poles, we believe that the crescentic shape does not affect the volume calculated in the proposed formula. Tapering poles of tumor nodule usually accounted for the height of the nodule in the formula we proposed, however, accounted for an insignificant tumor volume. To adjust the volume of a tumor nodule with tapering pole(s), we corrected the V by an empirical coefficient K of 2/3 for mid-prostate PZPAC associated with marked BPH and 1/2 for tumor nodules at the apex or base.

In summary, the volume of a tumor nodule is calculated by replacing \( D_1 \) in formula (A) with \( D_1 \) in formula (B) as follows:

\[
\text{Nodule volume} = 0.8 \times K \times D_1^2 \times D_2 \times \text{height/antero-posterior diameter of the prostate}
\]

In which:

- a) \( K = 1 \) for ovoid (small PAC < 6mm in diameter, TZPAC, most large PZPAC of GS > 3 + 4 and all PZPAC without associated BPH),
- b) \( K = 2/3 \) for a crescentic tumor (mainly PAC with GS < 4 + 3 and in the mid prostate with significant BPH),
- c) \( K = 1/2 \) for an ovoid nodule with tapering pole (PAC with GS < 4 + 3 and at the apex or the base of the prostate).

Graph 2 shows the correlation between the measured volume and calculated volume of the nodule with \( r^2 = 0.86, p \text{ value} < 0.001 \). The total volume of the carcinoma is the sum of volume of all tumor nodules.
Discussion

PAC occurs in the PZ in 70–75%, in TZ in 20–25%, and in CZ in 5% of cases. In this study, the shape of a tumor nodule is influenced by tumor grade and by the boundaries of the zone. For well and moderately differentiated PZ PAC (GS < 4 + 3), owing to its slow growth rate, the shape of the tumor nodule is influenced by the size of hyperplastic nodules and the location. We introduced the coefficient K to correct the effect of compression caused by these hyperplastic nodules.

Analysis of the height and volume of the tumor nodule, and the total tumor volume showed a good correlation with the current technique of measurement on each section of the prostate, particularly for tumors ranging from 1.5 to 3.0 cm³. Tumors below this range tended to have the calculated total volume lower than the “measured” one. This is probably due to the overestimation of the “measured” tumor volume. Our technique of calculation of the volume of PAC was likely to be accurate for small-volume tumors, particularly for tumors of less than 0.5 cm³ that were usually of ovoid shape suitable for applying the mathematical formula. Our proposed technique is simpler and less time consuming than our current technique or the current morphometric technique of measurement of tumor volume that requires the calculation of every surface area in the serial sections of the prostate. In addition, our proposed technique is supported by previous studies demonstrating a good correlation between the maximum tumor diameter – corresponding to D₁ in this study – and the prognosis of PAC \[18, 19, 22\]. However, the latter studies did not take into account the multifocality of the carcinoma and the second diameter – corresponding to D₂ in this study – as well as the shape of tumor nodule that may significantly account for the tumor volume.

In conclusion, by measuring the two greatest orthogonal diameters, D₁ and D₂, of the largest horizontal section of a tumor nodule, we were able to calculate the corresponding volume and, consequently, the total tumor volume. Our method of calculating tumor volume provides a means of tumor measurement with accuracy intermediate between arduous computer-assisted image analysis or grid morphometric work and the visual tumor estimation, which is likely subjective \[2, 12, 15, 21\].

References


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