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Dosimetric Consideration Of Transient Volume Enlargement Induced By Edema In Prostate Brachytherapy Seed Implants

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Abstract

Purpose

To investigate enlargement of prostate volume by edema during brachytherapy seed implantation and develop a nomogram model to calculate air-kerma strength (AKS) required for implantation of the enlarged transient prostatic volume.

Materials and Methods

The prostate volume was measured prior and after seed implantation using trans-rectal ultrasound imaging in the operating room to obtain volume enlargement. A nomogram model was developed that calculates AKS required for implantation of the enlarged transient prostate volume with optimal dose coverage.

Results

The measured prostate enlargement in this study was up to 60% of the initial volume. The effective prostatic volume enlargement was calculated for three isotopes: ^{125}I, ^{103}Pd and ^{131}Cs. The effective volume enlargement for ^{125}I implants was relatively small (< 10%) because of its long half-life. For ^{103}Pd and ^{131}Cs with short half-lives, additional AKS up to 20% and 30%, respectively, might be required to provide appropriate dose coverage of possible enlarged prostatic volumes.

Conclusions

Prostate volume enlargement should be considered to obtain optimal dose coverage particularly for short half-life isotopes such as ^{131}Cs and ^{103}Pd. The nomogram model developed in this work provides the AKS required for implants with a wide range of prostatic volume enlargements (5-100%) for three isotopes.

Keywords

prostate brachytherapy, nomogram, air-kerma strength, edema, volume enlargement

Introduction

Prostate brachytherapy seed implantation is becoming a more popular treatment technique for prostate carcinoma in early stages of the disease with low and intermediate risk patients[(1)] A considerable proportion of all prostate cancer patients are treated with brachytherapy implantation[(2)] The brachytherapy procedure can be used as the sole treatment technique or combined with external beam radiation therapy to boost the prostatic gland [(3)]. In comparison with external beam radiation, prostate brachytherapy has the advantage of treating prostate tumors locally by seed implantation of the gland using high doses with smaller irradiation of surrounding normal tissues compared to external beams.[(4)]

Despite the previously mentioned advantages of prostate brachytherapy, several technical issues are associated with the seed implantation procedure. These issues include edema of the prostate [(5-10)] and seed migration [(11-13)], which pose limitation on the dosimetric accuracy intended by the clinicians. Prostate edema results from surgical trauma by needle insertion and seed

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loading. Edema leads to the enlargement of the prostate volume which is difficult to account for during the seed implantation brachytherapy procedure. Even with image-guided intra-operative procedures [14,15], dosimetric calculation is performed on static ultrasound images and structures that are outlined prior to needle insertion and seed implantation assuming that prostate volume is unchanging. The volume of the prostate used for dosimetric evaluation of the intra-operative procedure does not usually include enlargement by edema. The edema resolves exponentially with time with an average resolution half-life of nearly 9.3 days[5], which is the time required for the prostate volume enlargement to shrink to half of its value at the peak of edema. Prostate volume enlargement may cause considerable dosimetric issues [16-19] particularly when using ^{103}Pd and ^{131}Cs seeds that have short decay half-lives of nearly 17 and 10 days, respectively. For example, ^{131}Cs seeds [19] have a decay half-life (9.7 days) comparable to the edema resolution half-life (9.3 days), and thus nearly 50% of the dose will be delivered to the enlarged prostate [16, 18, 20]. This might lead to significant dose discrepancies between the actual dose delivered and that intended by the clinician if the prostate volume enlargement is not considered.

In this work we have investigated variations of the prostate volume prior and subsequent to seed implantation in the operating room using US imaging. Further, we have developed a nomogram model to determine the increase in total AKS required for implantation of the enlarged transient prostate volume due to edema. This nomogram considers an effective prostate volume enlargement and increase in AKS required for implantation of the dynamic volume using three isotopes: ^{125}I, ^{103}Pd and ^{131}Cs.

Materials and Methods

Prostate Implantation Procedure

This study was conducted randomly on eleven prostate patients under an institutional-review-board protocol. The disease in these patients represented low and intermediate risk prostate cancer. Two-thirds of patients in this study were treated with sole prostate ^{125}I brachytherapy implants to doses of 145 Gy and one third received 110 Gy from brachytherapy combined with 45 Gy external beam radiotherapy. In our prostate brachytherapy procedure, intra-operative seed implantation guided with trans-rectal ultrasound imaging was performed on all 11 patients. The volume of the prostate was measured at the start of the procedure prior to needle insertion. Then, AKS required for implantation was calculated using a simple nomogram calculator [21]. Loose ^{125}I seeds (6711 Onco-seeds, Oncura, Arlington Heights, IL) were employed which were loaded using a Mick applicator (Mick Radio-Nuclear Instruments, Mount Vernon, NY) with US image-guidance.

After completion of the brachytherapy procedure, an ultrasound image set was acquired, the prostate was outlined and its volume was calculated. All contouring was done by one physician. The post-implantation US images included the enlargement of the prostate volume due to edema that is induced by needle insertion and seed implantation. The prostate volume enlargement is calculated from the difference in the volume of prostate between post and pre-needle insertion and seed implantation. We did not compensate for prostate volume enlargement in our brachytherapy implantation procedure. However, for the sake of this study, we have considered the increase in total AKS that will provide optimal dose coverage considering the transient prostate volume enlargement, retrospectively.

Prostate Transient Volume

The prostate was assumed to have a transient volume that decreases gradually as edema resolves with time post-implantation. A half-life time, τ_β, of 9.3 days for edema resolution was used[5] The initial volume of the prostate measured in the operating room prior to seed implantation was considered equal to $V_\circ$. The prostate enlarged maximal total volume was represented by V_T . The maximal enlargement of the prostate volume was given by $\Delta V_\circ = V_T - V_\circ$. The transient volume of the prostate, $V(t)$, after seed implantation as a function of time is given by the following equation:

$$V(t) = V_o + \Delta V(t) \quad (1)$$

where $\Delta V(t)$ is the dynamic prostate volume enlargement that is given by the following equation:

$$\Delta V(t) = \Delta V_o e^{-\beta_t t} \quad (2)$$

where $\Delta V(t)$ is the dynamic prostate volume enlargement that is given by the following equation.

where β =0.693 represents the edema resolution rate. τ_β

Seed AKS for the Prostate Transient Volume

The Anderson nomogram [22] used a linear equation based on dimensional averaging, d_α, of the prostate volume to calculate apparent radioactivity (old term for AKS) and seed spacing required for implantation according to the following: $A_o(mCi)=5d_\alpha(cm)$. This relationship was obtained from clinical data assuming that the prostate volume, V_o, is ellipsoidal:

$$V_o = \left(\frac{\pi}{6}\right) f_e d_a^3 \quad (3)$$

where d_α is the average diameter and f_e is the elongation factor of the ellipsoid. The Anderson nomogram was developed for retropubic prostate implants using uniform radioactive seed loading techniques. As more data became available, the initial ^{125}I nomogram was modified in order to account for peripheral loading and new treatment planning techniques[23-26]. Other nomograms were developed for new isotopes such as ^{103}Pd [24, 27] and ^{131}Cs [28]. Assuming f_e =1 and the average prostate diameter is equal to d_α, the modified AKS-volume nomograms for monotherapy using ^{125}I, and ^{103}Pd[24] delivering 145 Gy and 125 Gy are given in equations[4-5], respectively.

$$S_K^o(U) = 1.524 d_a^{2.2} \quad (4)$$

$$S_K^o(U) = 5.395 d_a^{2.56} \quad (5)$$

where $S_K^o(U)$ is AKS in U (μGym^2h^{-1}) [29].

For ^{131}Cs, the clinical nomogram data provided by the vendor [28] for mono- and combined therapy doses of 115 Gy and 85 Gy, respectively, was fit with a polynomial function. The best fitting curve is given by the lines in equation [6] for mono- and combined therapy, which produce all data points within 1% as shown in Fig. 1.

$$S_K^o(U) = 2.60V + 59.50$$
$$S_K^o(U) = 2.23V + 36.81 \quad (6)$$

The total kerma strength required for ^{131}Cs prostate implants depends linearly on the prostate volume plus a constant off-set as given in equation [6]. To obtain an equation for ^{131}Cs-AKS that depends only on the prostate volume similar to equations [4] and [5] for ^{125}I, and ^{103}Pd, respectively, equation [6] was rearranged and the volume of the prostate from equation [3] was substituted:

$$(S_K^o)_{net} = S_K^o(U) - 59.50 = 1.36 d_a^3$$
$$(S_K^o)_{net} = S_K^o(U) - 36.81 = 1.17 d_a^3 \quad (7)$$

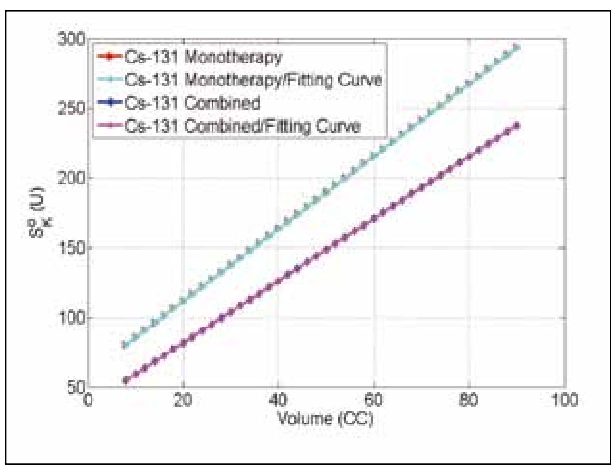


Figure 1: S^o_K -volume data for mono- and combined therapy 131Cs and the best-fitting curves.

Assuming the volume of the prostate remains stationary during the implantation, the dose required to achieve the clinical goals of dose coverage depends on the isotope used for seed implantation. For example, the dose coverage recommended by American Association of Medical Physics Task Group 43 [29] for prostate brachytherapy seed implants includes a D_{100} (dose that covers 100% of the volume) of 145 Gy for ^{125}I, and 124 Gy for ^{103}Pd. These doses depend on the prostate initial volume outlined on the static US images acquired prior to seed implantation, V_o , the total initial AKS implanted, $S^o{}_K$, and its decay rate, λ, with time as follows:

$$D = C\frac{\int_0^{\infty} S_K^o e^{-\lambda t}dt}{V_o^{\alpha}} \quad (8)$$

where C is a proportionality constant. α is the volume power given by equations (4, 5 and 7) for ^{125}I, ^{103}Pd and ^{131}Cs, respectively.

$$\alpha = \begin{cases} \frac{2.2}{3} & ^{125}I \\ \frac{2.56}{3} & ^{103}Pd \\ \frac{3}{3} & ^{131}Cs \end{cases} \quad (9)$$

The AKS of the implanted seeds decay exponentially, $S_K(t) = S^o{}_K e^{-\lambda t}$, with time post-implantation at a decay rate of $\lambda = \frac{0.693}{\tau_\lambda}$ where τ_λ is the half-life time for the seed decay. After integration in equation (8), we obtain the following simplified equation:

$$D = C\frac{1}{V_o^{\alpha}}\frac{S_K^o}{\lambda} = C\frac{S_K^o}{V_o^{\alpha}}\frac{\tau_\lambda}{0.693} \quad (10)$$

Rearrangement of equation (10), the initial AKS required for implantation is given by the following:

$$S_K^o = \frac{1}{C} D\, V_o^{\alpha}\frac{0.693}{\tau_\lambda} \quad (11)$$

Now, in the case of a changing prostate volume over time, equation (8) becomes as follows:

$$D = C\frac{\int_0^{\infty} S_K(t)dt}{(V_o + \Delta V_{eff}(t))^{\alpha}} \quad (12)$$

where $\Delta V_{eff}(t)$ is the effective volume of the prostate enlargement at time t post-implantation which represents the average volume of the prostate enlargement over a time period t assuming that it is stationary. The effective volume of the prostate is given by the following equation:

$$\Delta V_{eff}(t) = \Delta V_o \frac{\int_0^{t} e^{-\beta t}dt}{t} \quad (13)$$

Assuming that $S_K^{o\prime}$ is the total AKS required for implantation of a transient prostate with ΔV_o maximal volume enlargement, the dose-AKS relationship in equation (12) is given by:

$$D(t) = C\frac{S_K^{o\prime}\int_0^{t} e^{-\lambda t}dt}{(V_o + \Delta V_{eff}(t))^{\alpha}} \quad (14)$$

By integrating over time for both the seed decay and volume resolution in equation (14), the relationship between the total and initial AKS required for implantation of the transient and stationary volumes of the prostate is given by the following:

$$S_K^{o\prime} = S_K^o[1 + \frac{\Delta V_o}{V_o}\frac{\tau_\beta(1 - e^{-0.693\,t/\tau_\beta})}{0.693\,t}]^{\alpha}\,(\frac{1}{1 - e^{-0.693\,t/\tau_\lambda}}) \quad (15)$$

Equation (11) can be rearranged to give the ratio of total AKS required to implant the transient enlarged volume relative to the AKS required for the stationary prostate volume:

$$\frac{S_K^{o\prime}}{S_K^o} = [1 + \frac{\Delta V_o}{V_o}\frac{\tau_\beta(1 - e^{-0.693\,t/\tau_\beta})}{0.693t}]^{\alpha}\,(\frac{1}{1 - e^{-0.693\,t/\tau_\lambda}}) \quad (16)$$

Results

Figures 2 (a-c) show that the effective prostate volume enlargement, $\Delta V_{eff}(t)$, given by equation (13), decreased exponentially with time after seed implantation at a rate slower than instantaneous decrease in the prostate volume. $\Delta V_{eff}(t)$ represents an average volume of prostate enlargement over the time interval post-implantation that has passed so far. Considering an initial prostatic volume enlargement ΔV_o cm3, was about 5%, 18% and 28% of the maximal volume enlargement, $\Delta V_o cm^3$ $\Delta V_{eff}(t)$, after 5 half-lives of ^{125}I, ^{103}Pd and ^{131}Cs, respectively. Figures 3 (a-b) show that the prostate volume increased by up to 60% from its initial volume at the peak of edema, ΔV_o , which was measured immediately after seed implantation using US imaging.

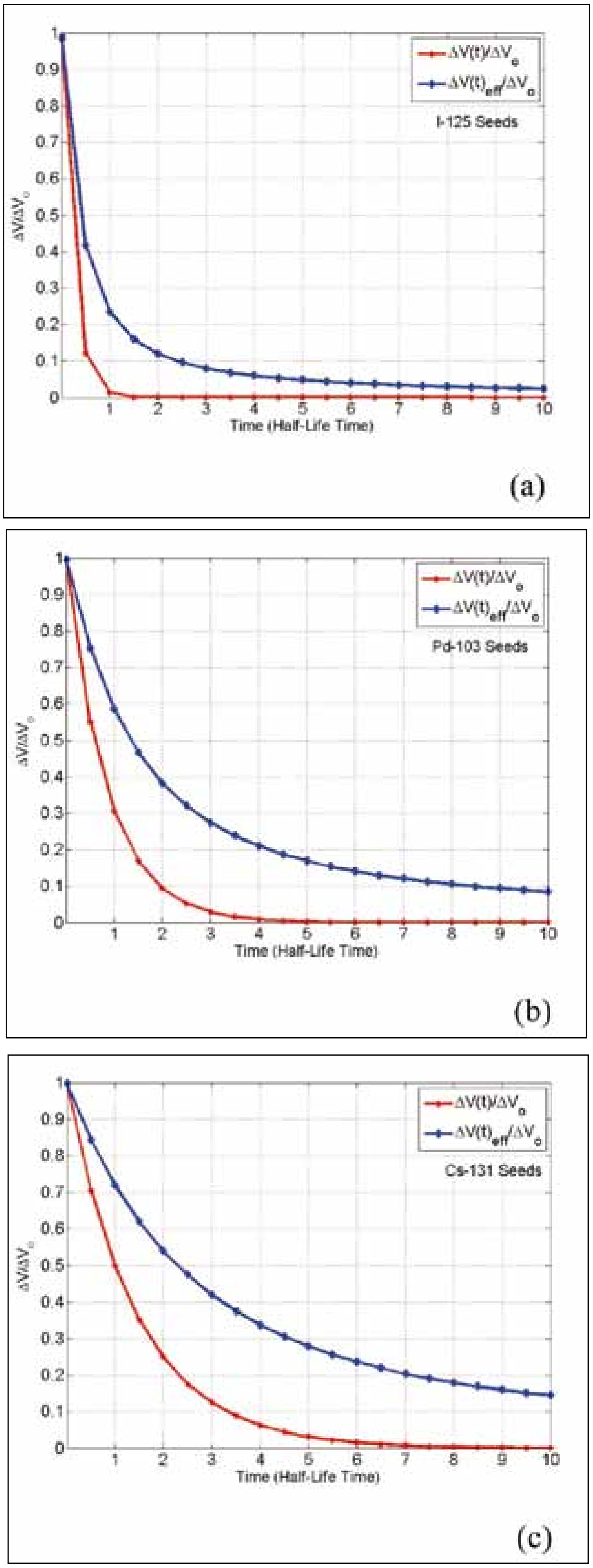


Figure 2: The ratio of the prostate volume enlargement, $\Delta V_{eff}(t)$, and the effective prostate volume enlargement, ΔV_{eff} , relative to the initial volume of the prostate, V_o , as a function of time post-implantation over a period of nearly 10 decay half-life for (a) ^{125}I, (b) ^{103}Pd, and (c) ^{131}Cs. An edema resolution half-life time of 9.3 days was used in the calculation of $\Delta V_{eff}(t)$.

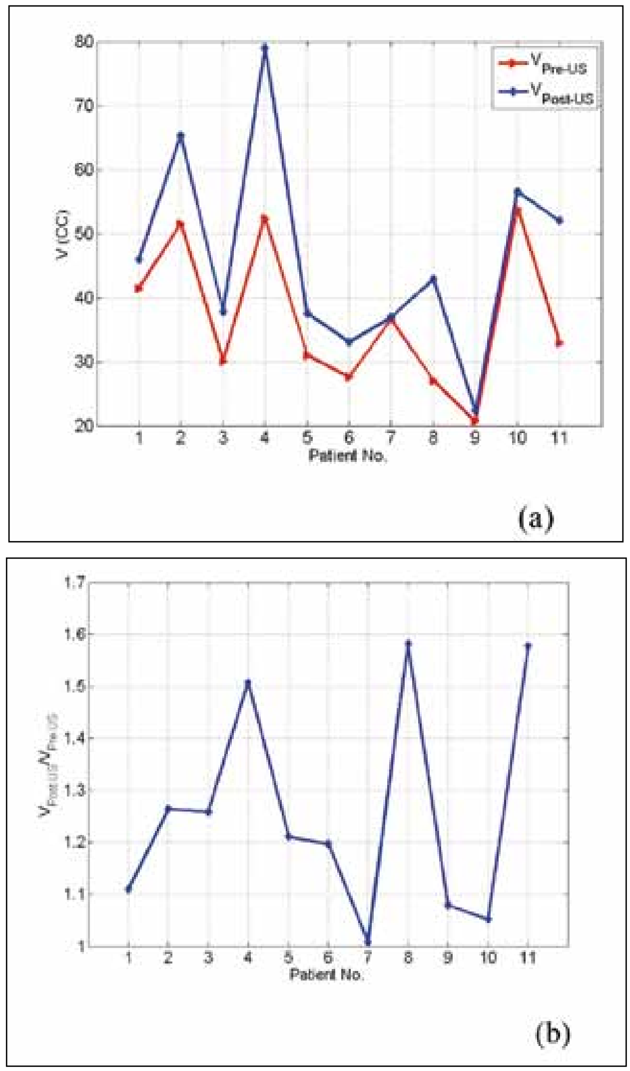
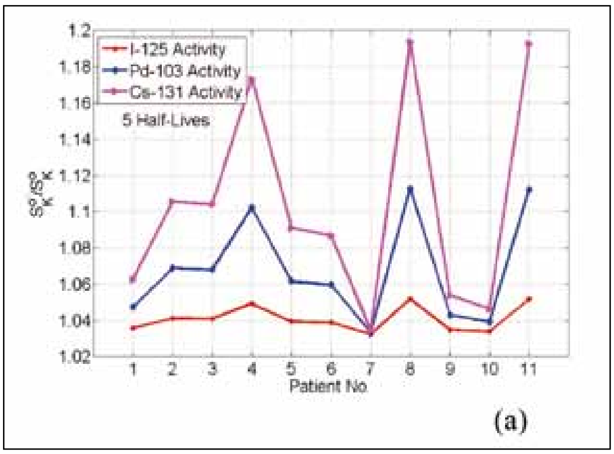


Figure 3: (a) The prostate volume measured from US images acquired at the start of the intra-operative procedure prior to seed implantation (data in triangles) and from US images at the end of the brachytherapy procedure (data in diamonds) (b) Ratio of the enlarged relative to initial volume of the prostate.

Figures 4 (a-b) show that additional AKS was required to implant the enlarged prostate volumes. The total initial AKS required depended on the radioactive isotope used for seed implantation. More AKS was needed for prostate seed implantation using shorter half-life isotopes. For example, patient 8, who had a maximal prostatic volume enlargement of nearly 60% as shown in Figure 3(b) required an increase in the initial total AKS of about 4%, 12% and 20%, when ^{125}I, ^{103}Pd and ^{131}Cs seeds were used for prostate brachytherapy implantation as shown in Fig 4(a), respectively. Further, Figures 4(a-b) show that the total required initial AKS depended on the time post-implantation at 5 or 10 half-lives, respectively. This resulted from the dependence of the effective prostate volume on time post-irradiation where it was smaller at longer times.



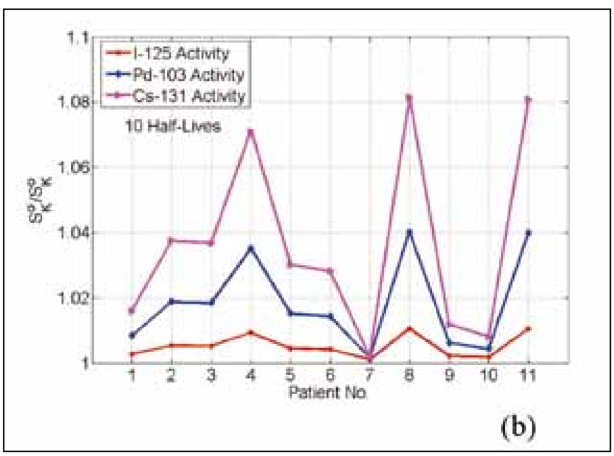
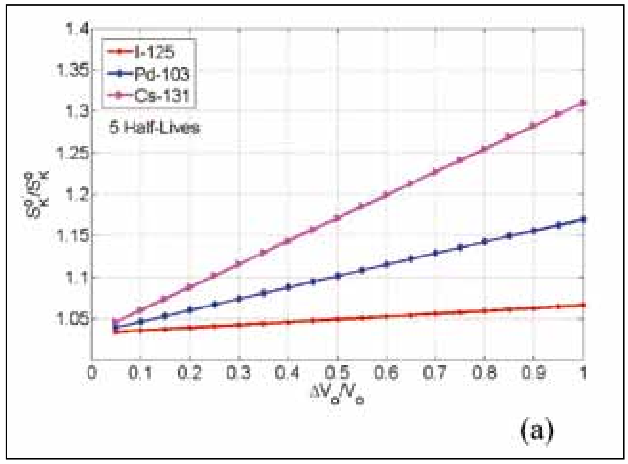


Figure 4: (a) Ratio of AKS required for seed implantation of the enlarged transient prostate volume relative to the stationary volume using ^{125}I, ^{103}Pd and ^{131}Cs considering effective volume at 5 decay half-lives considering an edema resolution half-life of 9.3 days. (b) Same as in (a) at 10 decay half-lives.

Figure 5 (a-b) shows that the ratio of the total AKS required for implantation as given in equation (16) depends on the ratio of the prostatic volume enlargement relative to the initial volume of the prostate, the isotope, and the time post-implantation. Figure 5(a) shows the total AKS ratio considering an effective volume at 5 half-lives when total AKS have decayed to about 3% of its initial value and Figure 5(b) at 10 half-lives when the total AKS have decayed to background level (< 1%).



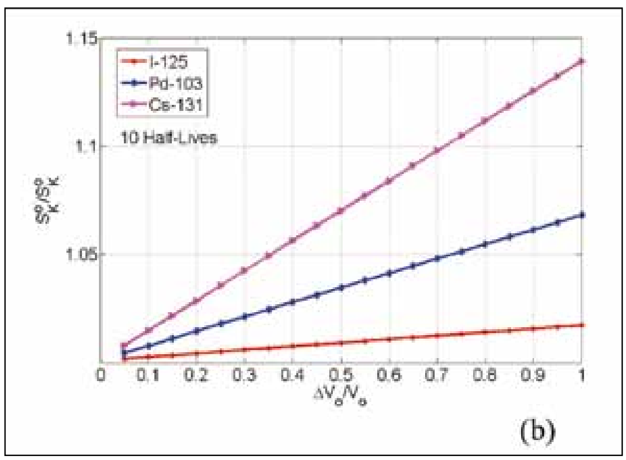


Figure 5: (a) A nomogram for AKS ratio versus prostate volume enlargement ratio for an effective prostate volume at 5 half-lives time using ^{125}I, ^{103}Pd and ^{131}Cs considering an edema resolution half-life of 9.3 days. (b) Same as in (a) at 10 half-lives time.

Discussion

The prostate volume enlargement due to edema from needle insertion and seed loading is not considered in volume studies that are performed usually prior to seed implantation using US images. Further, pre-plans or intraoperative plans are created on static US images acquired prior to prostate enlargement during the seed implantation brachytherapy procedure. The AKS required for implantation is calculated using a stationary prostate volume which usually fails to consider volume enlargement. In this work, we measured volume enlargement as high as 60% at the end of the implantation procedure that is not accounted for in implanted AKS. This may lead to significant discrepancies in achieving the intended dose coverage which may affect the outcome of tumor control. Contrary to seed implantation of the enlarged volume of the prostate after needle insertion as performed with ^{131}Cs seed [18, 30], the effective volume introduced in this work consider a transient volume that changes with time. Implantation of the maximal enlarged prostate volume without considering edema resolution with time may result significant higher doses leading to urinary and rectal complication once the prostate shrinks back to its baseline volume. The nomogram model here provides a tool to calculate extra AKS required to compensate dosimetricaly for the transient volume enlargement.

CT images acquired nearly 4 weeks after seed implantation are used for quality assurance of the brachytherapy procedure. However, the prostate volume measured by CT does represent neither the enlarged nor the initial volume of the prostate. In this work we propose measurement of the prostate volume at the end of the brachytherapy procedure in the operating room using US imaging and use of these images to evaluate prostatic gland enlargement. The model developed here provides a nomogram that can be used to obtain the increase in AKS required for implantation of the enlarged volume. The approach described here requires nearly 30 minutes additional time on the regular procedure. This includes US image acquisition, modification of the contours to include the enlarged volume of the prostate and implantation of extra seeds to ensure dose coverage. The seeds should be implanted intra-operatively to fill up seed gaps in the enlarged prostate until optimal dose coverage has been reached.

Another problem in a brachytherapy procedure that considers the enlarged prostate volume is the preparation for having enough AKS available in the operating room. The initial volume of the prostate is usually measured ahead of time using the volume study, and then total AKS required for implantation is ordered. Treatment planning or an AKS-volume nomogram is used to obtain the total AKS required for implantation. Usually, this total AKS and 10% extra are ordered in the preparation for the seed implant. However, the prostate volume enlargement is known only in the operating room after needle insertion and the seed implantation. The AKS required to consider enlarged volume may exceed 10% additional AKS. As shown in Figure 5, at least 7%, 20% and 30% extra AKS should be prepared for ^{125}I, ^{103}Pd and ^{131}Cs seed implantation brachytherapy procedures, respectively. Thus, for ^{125}I, the increase in AKS required for implantation of an enlarged prostatic volume that may have doubled its initial volume due to edema can still be accounted by the 10% extra seeds that are ordered ahead of time. However, for ^{103}Pd or ^{131}Cs seeds, 10% extra seeds might not be enough to provide dose coverage for prostatic volume enlargement.

The effective volume, ΔV_{eff}, introduced in this work is dependent on the isotope used for implantation. Over five half-lives of ^{125}I (nearly 300 days), edema increases the initial prostate volume in average by 5% (Fig. 2(a)). While, five half-lives of ^{103}Pd (85 days) and ^{131}Cs (50 days), the corresponding ΔV_{eff}'s are 18% and 28% of the static prostate volume as shown in Figs 2 (b-c), respectively. Thus, prostates that are implanted with ^{131}Cs and ^{103}Pd have larger ΔV_{eff} than those implanted with ^{125}I. This explains significant increase in total AKS required for implantation of the enlarged prostate using these isotopes.

Conclusions

In this work, we have developed a model that calculates the increase in AKS required to achieve optimal dose coverage for the enlargement of the prostate volume by edema induced by needle insertion and seed implantation during the prostate brachytherapy procedure. We used effective enlarged prostatic volumes in the range from a few percent to 100% at 5 and 10 half-lives for three isotopes: ^{125}I, Pd-125 and ^{131}Cs considering edema resolution half-lives of 5, 9.3 and 20 days. ^{125}I seeds have a relatively long half-life and thus small effective prostatic volume enlargement by edema. The AKS increase required for implantation is only about 7% for 100% volume enlargement which is still can be covered with the extra 10% AKS that is usually ordered before implantation day. However, for short half-life isotopes such as ^{131}Cs and ^{103}Pd, enough extra AKS of 30% and 20%, respectively, should be on hand for the brachytherapy procedure ahead of time to provide appropriate dose coverage of possible enlarged prostate volumes.

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