Original article

I-125 seed calibration using the SeedSelectron® afterloader: a practical solution to fulfill AAPM-ESTRO recommendations

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Abstract

Purpose: SeedSelectron® v1.26b (Nucletron BV, The Netherlands) is an afterloader system used in prostate interstitial permanent brachytherapy with I-125 selectSeed seeds. It contains a diode array to assay all implanted seeds. Only one or two seeds can be extracted during the surgical procedure and assayed using a well chamber to check the manufacturer air-kerma strength (S_K) and to calibrate the diode array. Therefore, it is not feasible to assay 5-10% seeds as required by the AAPM-ESTRO. In this study, we present a practical solution of the SeedSelectron® users to fulfill the AAPM-ESTRO recommendations.

Material and methods: The method is based on: a) the SourceCheck® well ionization chamber (PTW, Germany) provided with a PTW insert; b) n = 10 selectSeed from the same batch and class as the seeds for the implant; c) the Nucletron insert to accommodate the n = 10 seeds on the SourceCheck® and to measure their averaged S_K. Results for 56 implants have been studied comparing the S_K value from the manufacturer with the one obtained with the n = 10 seeds using the Nucletron insert prior to the implant and with the S_K of just one seed measured with the PTW insert during the implant.

Results: We are faced with S_K deviation for individual seeds up to 7.8%. However, in the majority of cases S_K is in agreement with the manufacturer value. With the method proposed using the Nucletron insert, the large deviations of S_K are reduced and for 56 implants studied no deviation outside the range of the class were found.

Conclusions: The new Nucletron insert and the proposed procedure allow to evaluate the S_K of the n = 10 seeds prior to the implant, fulfilling the AAPM-ESTRO recommendations. It has been adopted by Nucletron to be extended to seedSelectron® users under request.

J Contemp Brachyther 2012; 4, 1: 21-28
DOI: 10.5114/jcb.2012.27948

Key words: brachytherapy, prostate, afterloader, selectSeed.

Purpose

SeedSelectron® v1.26b (Nucletron BV, Veenedaal, The Netherlands) is an afterloader system used in prostate interstitial permanent brachytherapy with ^{125}I selectSeed™ seeds. This system has been described and technically evaluated by Rivard *et al*. [1]. The system is composed of an array of diodes to assay all implanted seeds. Because seeds are on presterilized cartridges, only one or two seeds can be extracted during the surgical procedure and then independently assayed by physicist with a calibrated well chamber to check the manufacturer air-kerma strength (S_K) and to calibrate the diode array. This is done during the intraoperative procedure once the interactive planning has been completed, assuming the manufacturer air-kerma strength value.

The quality assurance (QA) procedure of the American Association of Physicist in Medicine (AAPM) and European Society for Radiotherapy and Oncology (ESTRO) recommendations [2,3] state that:

1) For each multi-source implant with a large amount of loose seeds, AAPM recommends that a random sample containing at least 10% of the seeds should be assayed. For seeds purchased in a sterile configuration, AAPM recommends purchasing and assay a number of non-sterile loose seeds equal to 5% of the total number of seeds or five seeds, whichever is fewer.
2) AAPM further recommends that (a) if the mean value of users independently measured seed strength for the assay batch disagrees with the manufacturer's data by more than 3%, the users need to investigate the origin of the disagreement; (b) an unsolved disagreement exceeding 5% warrant reporting to the manufacturer; (c) the measured strength of each individual seed should be within 5% of the measured mean for the batch.

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Received: 10.01.2012
Accepted: 22.02.2012
Published: 31.03.2012

In order to fulfil the AAPM-ESTRO recommendations there are some critical points in the current seedSelectron® afterloader procedure:

1) Practical difficulties to assay the required seed quantity (5-10%). Since seeds are included in a sterilized cartridge, it is not possible to fulfil the AAPM-ESTRO recommendations about the size of the sample of seed assayed and the manufacturer certificate air-kerma strength value comparison.
2) The low accuracy of the diode system.
3) The fact that planning is done assuming the manufacturer air-kerma strength without having a clear option of updating this value in the Treatment Planning System (TPS).

The manufacturer claims that with the SeedSelectron® diode array the system fulfils the AAPM-ESTRO recommendations. This is in contradiction with the large diode uncertainty obtained in clinical practice. Moreover, there is a warning in the SeedSelectron® software about the diode readings indicating that they are just "indicative". According to the manufacturer Instruction Manual[1], just one seed is required from the sterilized cartridge to be assayed with the calibrated external well ionization chamber and to calibrate the array of diodes. Typically, the medical physicist compares the air-kerma strength she/he measures with that given in the manufacturer certificate, facing the problem that it is not clear what action level should be applied in the eventuality that both values are significantly different.

Carmona *et al*. [4] used the typical statistical methods of quality control processes to analyze the air-kerma strength stability, provided in the certificates of Rapid Strand from Amersham (Amersham, UK) for different shipments of seeds. They measured individually the air-kerma strength of ten seeds (one rapid strand) for five shipments, i.e., a total of fifty seeds. They concluded that the seeds can be considered homogeneous and their air-kerma strength can be compared with that specified by the manufacturer. The systematic deviation between their measurements and the values provided by the supplier was 1.3%.

Ramos and Martínez [5] proposed a new sampling method in which the number of seeds to be measured (n) in relation to the total sample size (N), will be set beforehand according to an a priori statistical level of uncertainty. Defining a tolerable level of uncertainty ($\delta_{1-\alpha}$) at a level of statistical confidence (1-α), n is deduced using as variance of the sample the one of the historical records. The results are based on the assumption that the air-kerma strength follows a normal distribution. To demonstrate this, the air-kerma strength of each seed was corrected to ensure that the average air-kerma strength of its sample remained the same. In this process 2030 results (^{125}I 6711 seed model supplied by Amersham) were collected and analyzed using a normal plot.

Rodríguez *et al*. [6] studied the air-kerma strength distribution of sterile ^{125}I seeds provided by IBt-Bebig (IBt-Bebig GmbH, Germany) and they deduced an adequate size of control sample. They measured 200 seeds from 56 batches and they found that the air-kerma strength distribution can be described by a rectangular distribution convolved with a Gaussian function. The width of the rectangular distribution is related to the width of the "activity classes" in which IBt-Bebig classifies its seeds and the Gaussian function takes into account the uncertainties in the measurement of the air-kerma strength. The measured distribution complies with the AAPM-ESTRO tolerance of the maximum deviation of the air-kerma strength of individual seed (5%). They concluded that with samples of 3 seeds they can assert (with a confidence level of 95%) that the batch belongs to the specified class if the difference between the sample average of the air-kerma strength and the reference value for the class is less than 2.5%.

Santos *et al*. [7] measured the air-kerma strength of 364 selectSeed™ from 49 implants and studied the deviations between the measured air-kerma strength of each seed and the value certified by the supplier. The differences between the mean value of the air-kerma strength they measured and the certified value for the 49 shipments was 0.51% ± 2.4% (k = 1). For the N = 364 seeds the difference is 0.61% ± 3.1% (k = 1).

Yue *et al*. [8] proposed and used a method to quantify the assay process of seeds. The results showed that the quality of a seed assay process was dependent on the measured seed strength distribution and the number of assayed seed (n). Its dependence on the total number of seeds (N) becomes statistically insignificant if N is large enough. The assay process can be determined by the obtained assay information, instead of predetermined percentage of total seeds to be used. It was also found that the use of the manufacturer stated S_K value may possibly lead to larger uncertainty in strength accuracy, unless the strength stated by the manufacturer is the measured mean value of all ordered seeds.

The purpose of the present work is to describe a practical solution to be adopted in clinical routine by the seedSelectron® users to fulfil the AAPM-ESTRO recommendations. To this end, we have developed an insert (named as Nucletron insert in this study) and a procedure in collaboration with Nucletron which provides a separate non sterile container with n = 10 selectSeed™ seeds belonging to the same batch and class as the rest of the seeds for the implant. So, the AAPM-ESTRO recommendation that "a random sample containing at least 10% of the seeds should be calibrated", is fulfilled for a typical shipment of N = 100 seeds. Measuring the n = 10 seeds at once we deduced the average air-kerma strength of the seeds in a fast and simple way using the Nucletron insert developed in the present work. An uncertainty analysis of the process was done. In addition, a statistical analysis of the air-kerma strength values assayed by the authors in the clinic is included.

Material and methods

Afterloader and current procedure

The Fully Integrated Real-time Seed Treatment (FIRST™) system by Nucletron has been available since 2001and being currently used in a significant number of Hospitals, mainly in Europe, as the unique automatic afterloading system for prostate seeds.

This system has been intensely described by Rivard *et al*. [1]. In brief, this system is an interactive intraopera-

[1] *seedSelectron User Manual v1.1 Nucletron Part#190.001ENG-01*

tive treatment planning and delivery system for prostate seed brachytherapy. It is composed by a TPS (SPOT-PRO) and the afterloader named SeedSelectron®. Once the interactive planning is finalized, the plan is exported to the SeedSelectron®. The system automatically builds the trains with the planned seeds/spacers combination from sterilized seeds (^{125}I selectSeed™) and spacer cartridges. The SeedSelectron® incorporates a sixteen diode array to verify the build sequence and assay the individual seed strength.

According to the manufacturer, the diodes can be calibrated using one seed of the set which S_K is measured with a well chamber traceable to an Accredited Dosimetry Calibration Laboratory (ADCL). This calibration factor, introduced by the user, is translated to the sixteen diode array. The array confirms the build sequence of seeds and spacers as the unit assembles elements to be loaded into a needle and measures the seed strength of all seeds. Diode response tolerances are set to different default colours/levels depending on the difference between the S_K of the seed, used to calibrate the diodes and diode-measured S_K of a seed: green if difference is within ± 15%, yellow if 15% < |difference| < 25%, and red if |difference| > 25%. The default levels can be changed with the aid of the manufacturer. If the |difference| > 50% of the expected reading S_K, the system should assign a spacer to that position.

Proposed method

The new procedure proposed in this study to fulfil the AAPM-ESTRO recommendations is based on the following elements:

1) A well-ionization chamber (SourceCheck PTW, Germany) provided with an insert (PTW insert); the chamber is 220 mm long and provides a uniform sensitive area (sweet spot) of approximately 120 mm[2].
2) A separate non sterile container with n = 10 selectSeed™ from the same batch and class as the seeds for the implant.
3) An insert (the Nucletron insert, developed in this study) with a slot is used to accommodate the n = 10 separate seeds on the SourceCheck and to perform a single measurement deducing the averaged air-kerma strength per seed, $\overline{S_K}$.

An agreement has been signed with Nucletron to obtain a separate non sterile container with n = 10 seeds for all users under request. Nucletron will certify that these 10 seeds come from the same batch and class that the seeds included in the cartridge for the implant. These n = 10 separate seeds set could be measured even several days prior to the implant.

In order to optimize the measuring procedure of the n = 10 seeds, the Nucletron insert (Fig. 1A) is fitted externally to the wall chamber plate, similarly to the already existing holders to assay strands on this chamber[2]. A slot in the Nucletron insert allows to allocate the 10 seeds at the same time.

Using the PTW insert and the calibration factor of the SourceCheck chamber f^{PTW}, the user calculates the air-kerma strength of a seed by $S_{K,i} = f^{PTW} R^{PTW} \varphi(p,T)$, where R^{PTW} is the reading and $\varphi(p,T)$ accounts for climatic conditions.

With the Nucletron insert mounted (see Fig. 1B) and the n = 10 seeds distributed into the slot, we performed a single measurement deducing the average reading per seed, $R^{Nucletron}$ of the set. Consequently, the average air-kerma strength per seed of the set is estimated by:

$$\overline{S_K} = f^{PTW}\left(R^{Nucletron} \times f^{PTW}_{Nucletron}\right) \varphi(p,T) \quad (1)$$

The relation between the readings with the PTW insert and the Nucletron insert, $f^{PTW}_{Nucletron}$ is deduced measuring several times a selectSeed™ with both inserts and taken the ratio of the averaged values:

$$f^{PTW}_{Nucletron} = \overline{R^{PTW}} / \overline{R^{Nucletron}}$$

Validation of the proposed method

A NIST standard seed of S_K = 1.549 U (1 U = 1 μGyh^{-1}m^2) at the date of our measurements, with uncertainty of 1.68% (coverage factor k = 2), was used to calibrate (f^{PTW})

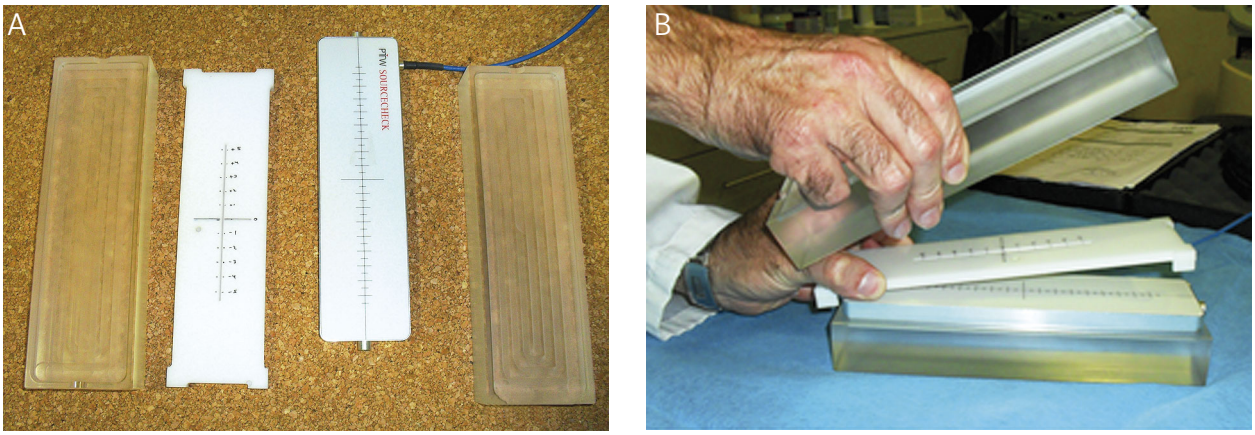

Fig. 1. A) Left-right: PMMA block, Nucletron insert to allocate the 10 selectSeed™, PTW SourceCheck (without the PTW insert), PMMA block (B) Mounting the set-up. Bottom-top: PMMA block + SourceCheck + Nucletron insert + PMMA block

[2] *SourceCheck Application Note 62420800 PTW Freiburg*

the SourceCheck chamber with the PTW insert provided with the chamber.

The SourceCheck chamber profile response was obtained locating the calibrated seed at 1 cm intervals along the slot in positions P +5, +4, …, +1, 0, -1, …, –5, as indicated in Fig. 1A. The insert was mounted as indicated in Figure 1B. The sweet-spot length of the chamber was compared with the manufacturer specifications.

In order to obtain $f^{PTW}_{Nucletron}$, the calibrated selectSeed™ was located in the centre (P = 0) of the slot of the Nucletron insert (with the PTW insert removed).

A study was done to check that our method with the Nucletron insert provides compatible results with the individual measurement of each one of the n = 10 seeds, using the PTW insert ($\overline{S_{K,i}} = \sum_{i=1}^{10} S_{K,i}$) or calculating its averaged value from a single measurement with the Nucletron insert ($\overline{S_K}$).

Ten non-sterile seeds accompanying the seeds for the implant of 56 patients were measured using the Nucletron insert and its $\overline{S_K}$ value compared with the manufacturer S_K^{Ci} in the certificate and with the air-kerma strength of a single seed extracted and measured during the implant ($S_{K,implant}$). The distribution of ($S_{K,implant}$) was fitted to the model of Rodríguez *et al.* [6] (see appendix).

Results

Using the NIST calibrated selectSeed with the PTW insert, the calibration factor of the SourceCheck resulted $f^{PTW} = 1.1112 \frac{U}{pA} \pm 0.84\%$ (k = 1). Uncertainty combines the Type A uncertainty (0.025%) of ten measurements ($\overline{R^{PTW}}$) and the S_K uncertainty of the calibrated seed.

By means of ten measurements with the NIST calibrated selectSeed™ located at P = 0 into the slot of the Nucletron insert (and removing the PTW insert), $\overline{R^{Nucletron}}$ with 0.053% (k = 1) Type A uncertainty, the relation between both readings was deduced: $f^{PTW}_{Nucletron} = 1.8789 \pm 0.060\%$ (k = 1) (see below for a correction to this value).

Chamber profile response

SourceCheck Chamber profile response with the Nucletron insert was obtained with the calibrated seed and it is shown in Fig. 2.

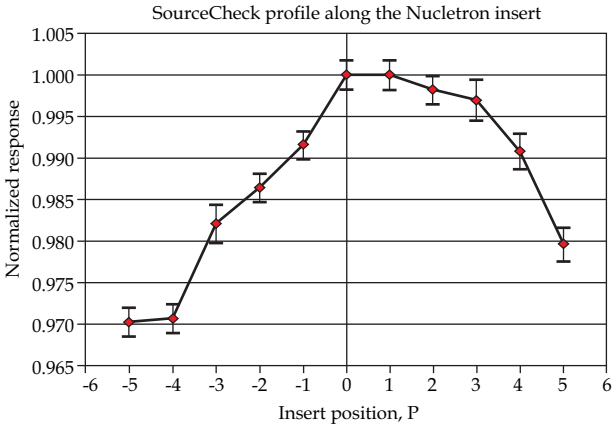

Fig. 2. Response of the chamber along the seed positions P on the Nucletron insert. Error bars represent one standard deviation (k = 1) of the mean

The largest difference in chamber profile response with respect to the value at P = 0 is +3% for P = –5. Despite the small profile asymmetry, the chamber profile response resulted within ± 1.5% of the mean response for a length of 10 cm in agreement with the specifications of PTW. This profile should be verified by each SourceCheck user.

In order to check whether the use of $f^{PTW}_{Nucletron}$ (deduced for P = 0 for all seed positions) in the slot of the Nucletron insert without taken into account the response of chamber in Fig. 2 was accurate enough, we compared for an implant the average $\overline{S_{K,i}}$ performing individual measurement of the n = 10 separate seeds with the PTW insert, with the $\overline{S_K}$ value obtained with the Nucletron insert using the method proposed. We attained the following results: $\overline{S_{K,i}}$ = 0.424 U ± 1.0% (k = 1), $\overline{S_K}$ = 0.429 U ± 0.87% (k = 1). As expected, taking into account data in Fig. 2, $\overline{S_K}$ was higher than $\overline{S_{K,i}}$, but the difference was only 1.1%. To obtain a better agreement $f^{PTW}_{Nucletron}$, should be reduced by 1.1% to take into account the response of the chamber in Fig. 2 and considering that the user distributes the 10 seeds randomly along the slot (avoiding superposition between them). The final value was: $f^{PTW}_{Nucletron} = 1.8582 \pm 0.058\%$ (k = 1).

Finally, to evaluate the influence of the 10 seed distribution within the slot, we repeated the measurement of the 10 seeds with the Nucletron insert changing the seeds distribution along the slot and we obtained that the final uncertainty was: ($\overline{S_K}$ = 0.429 U ± 0.88% (k = 1).

Consequently, the proposed simplified method using the $\overline{S_K}$ attained with the Nucletron insert is compatible within uncertainties with the $\overline{S_{K,i}}$ obtained by individual measurement of each of the 10 seeds using the PTW insert. The uncertainty associated with a single measurement of the Nucletron insert was: $\sigma_{Nucletron}$ = 0.88% (k = 1).

Results of 56 patients

In the present study, we have measured $\overline{S_K}$ for 56 implants and $S_{K,\,implant}$ for 48 implants. Figure 3 shows the manufacturer S_K with $S_{K,\,implant}$ and with $\overline{S_K}$. The advantage of using the Nucletron insert reflects on the fact that only in two implants $\overline{S_K}$ falls (barely) outside the [–4%,4%] range of the class, while $S_{K,implant}$ was outside the range in 22 implants.

We demonstrate in the appendix by analysing a large number of S_K measurements from Santos *et al.* [7] that the final distribution of S_K corresponding to a particular class is given by the Rodríguez *et al.* model [6] in equation (A.2).

In Fig. 4A, we present the experimental distribution of $(S_{K,\,implant} - S_K^{Ci})/S_K^{Ci}$ and their fit to equation (A.2). As expected, $\sqrt{(\sigma^M)^2 + (\sigma^U)^2} = \sqrt{(1.5)^2 + (1.0)^2} = 1.8\%$ match with the fitted value of σ = 1.8% ± 0.7%. For the fitted distribution $\sum$ = 2.9% and considering only σ^U it is $\sum$ = 2.8% (see appendix). The conclusion is that there is a systematic deviation of Δ = –2.1% ± 0.7% between the user and the manufacturer S_K values.

Figure 4B shows the distribution of the $\overline{S_K}$ measuring 10 seeds with the insert for 48 implants. In this case, we assumed that the distribution of the means is a normal distribution (see appendix). In this case σ_{10} = 1.7% ± 0.7% is consistent within uncertainties with the expected value of

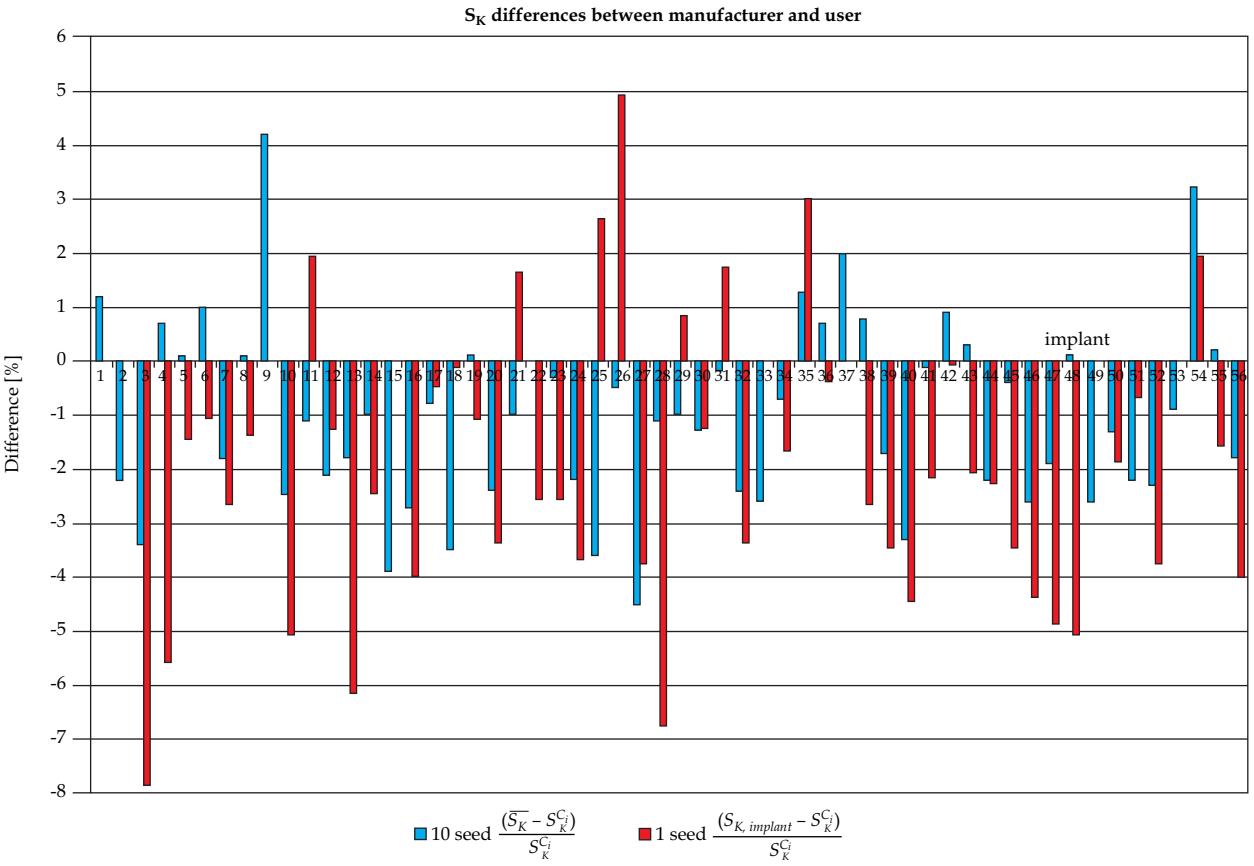

Fig. 3. $(S_{K,\,implant} - S_K^{Ci})/S_K^{Ci}$ and $(\overline{S_K} - S_K^{Ci})/S_K^{Ci}$ for 56 implants. In some implants the measurement of one seed was not done because all seeds were used in the implant

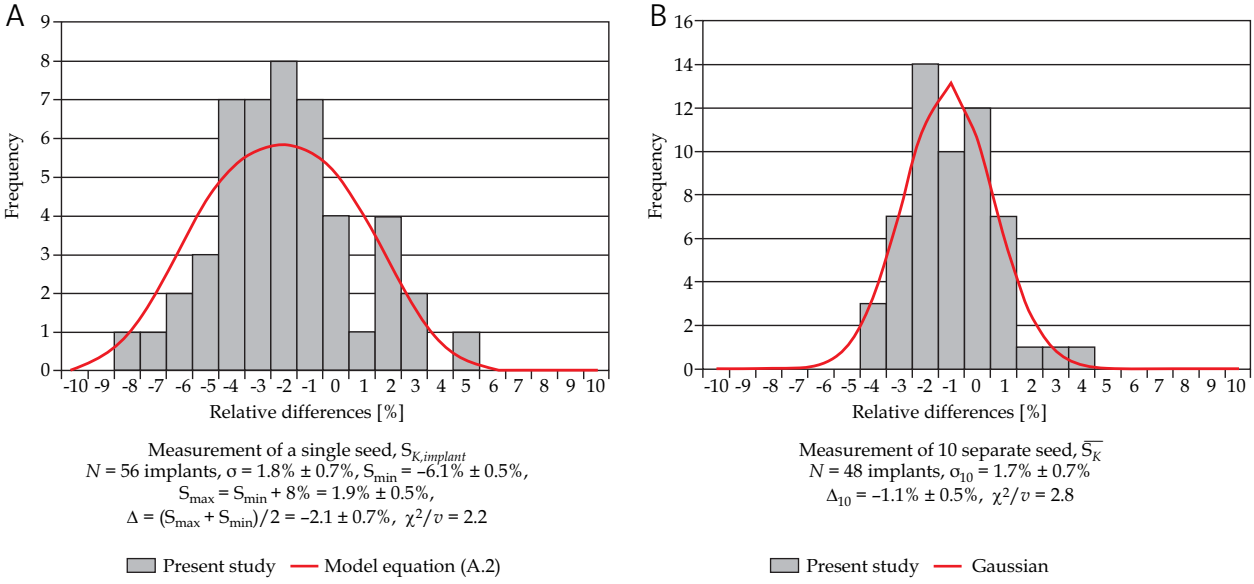

Fig. 4. A) $(S_{K,\,implant} - S_K^{Ci})/S_K^{Ci}$ for 56 implants has been fitted to the model of equation (A.2). The fitted parameters are σ and S_{min}. The model assumes one measurement for both the manufacturer and the user. B) $(\overline{S_K} - S_K^{Ci})/S_K^{Ci}$) distribution for 48 of 56 implants. The fitted parameters are σ_{10} and Δ_{10}

$\sqrt{\left(\frac{\sum}{\sqrt{10}}\right)^2 + (\sigma_{Nucletron})^2} = 1.3\%$. The systematic deviation between user and the manufacturer indicated by $\overline{S_K}$ data is $\Delta_{10} = -1.1\% \pm 0.5\%$, lower than the value indicated by the $S_{K,implant}$ data.

Discussion

As already mentioned, the current diode array system of the SeedSelectron® is not sufficiently accurate. This conclusion was also stated by Rivard *et al*. [1] which concluded that the generous settings for seed S_K measurement tolerances are due to the deficiencies of the system in reporting the correct S_K of the seed, even calibrating the diode system for every new seed batch, which generally means a new calibration for each patient.

We adjusted the tolerance values in the system to be closer to 3-5% values, currently recommended by AAPM-ESTRO with bad results. As commented previously, into the SeedSelectron® application it is possible to access the diode readings once the plan has been executed and the warning legend indicates that "values of this table are only indicatives". With the simple method proposed in this study, users can fulfill efficiently the AAPM-ESTRO recommendations avoiding current situations derived from just one seed available for measurement. In our experience, we are faced with S_K deviation for individual seeds up to 7.8%. However, in most cases, S_K is in agreement with the manufacturer value. Deviations are due to the combination of the dispersion within the class and uncertainty in the measurement. The role of the measurement of one seed of the sterilized cartridge on the operation room is still required. This is because if it is not done, the afterloader does not check the train composition regarding seeds/spacers. The method proposed in this study will be valid even if a more accurate array on this afterloader is implemented in the future [9], because it allows to evaluate the S_K and compare it to the manufacturer value previously to a surgical procedure.

Conclusions

We developed a practical solution to be adopted in clinical routine by the SeedSelectron® users to fulfil the AAPM-ESTRO recommendations. The new Nucletron insert and the procedure proposed, allows to evaluate the seeds S_K prior to the intraoperative procedure. This will avoid the diode limitations of the SeedSelectron® and the dispersion/uncertainty involved in single seed assay. The Nucletron insert allows to perform efficiently the mean S_K of the non-sterile 10 seeds set. This procedure solves efficiently the fulfilment of the AAPM-ESTRO recommendations and it is available to all SeedSelectron® users under request to Nucletron.

Appendix A

User S_K distribution of seeds of the same class

According to Yue *et al*. [8], the recommendations concerning the calibration of seeds employed in brachytherapy can be established from the S_K distribution produced by a particular manufacturer, independently of the number of seeds included in certain shipping. Despite this, the AAPM-ESTRO recommendations are still dedicated to the classic approaches in which one must test a given number of seeds depending on the total number of seeds that are used in a particular brachytherapy procedure.

For the present case, the distribution of S_K provided by the manufacturer can be established in an adequate way and afterwards it is possible to give specific comments about the verification process.

The manufacturer defines classes C_i to classify seeds in such a way that if the central value of the class i is $S_K^{C_i}$ it covers the range of $S_K^{C_i} \pm 4\%\ S_K^{C_i}$ (i.e. each class cover an 8% interval decay, the decay of ^{125}I in a week). The manufacturer classifies the selectSeed™ seeds in 16 classes. After one week, the seeds belonging to a class go through the next one. Nucletron-Isotron provides a certificate in which the average S_K of the "class" belongs to the seeds contained in the cartridge ordered for a certain date.

Due to the neutron activation process of the seeds and their classification in classes, it can be assumed that the distribution of the seed strengths inside a class is uniform. This can be justified assuming that the S_K distribution of a large amount of seeds should follow a normal distribution. If we classified them in classes (say 16) it is reasonable to assume that in a class the distribution is uniform (i.e., we approximate the distribution by a histogram with bins width equal to the class range).

Let us assume the following typical scenario: the manufacturer (Isotron) measures a selectSeed™ once and obtain S_K^M and classifies it in the class C_i if the measurement results inside the range of $S_K^{C_i} \pm 4\%\ S_K^{C_i}$. If the manufacturer measurement a standard deviation σ^M, performing only one measurement, the result should be expressed as $S_K^M \pm \sigma^M$ ($k = 1$). The manufacturer delivers $N = 100$ seeds of the same batch and class to a hospital and in a certificate it gives as mean value of the seeds $S_K^{C_i} \pm 4\%\ S_K^{C_i}$.

The user has an ionization chamber calibrated by a primary or secondary laboratory with standard deviation σ^U. With only one measurement of a seed with this device, the result should be expressed as $S_K^U \pm \sigma^U$ ($k = 1$).

Following the seed manufacturing process, including all uncertainties associated to the way how a certain seed reaches a particular S_K, it could be assumed that the S_K distribution of a given batch is Gaussian-like. This had been checked in some cases [5]. The manufacturer does not give information about this issue and the indication of only one interval of activities determined by the ^{125}I decay forces us to assume a uniform distribution of S_K for the set of seeds forming a given class. In addition and due to the uncertainty of the measuring device used by the manufacturer to classify the seeds and the measurement done by the user, the final distribution of S_K corresponding to a particular class will be the result of the convolution of the distribution corresponding to the classification criteria (uniform) and the uncertainty distribution associated to the measuring device of the manufacturer and the user (Gaussian) [6]. This can be expressed mathematically as:

$$p\,(S_K) = \int_{-\infty}^{+\infty} C_{S_{min}}^{S_{max}}(t)\; N\,(S_K - t, \sigma)\; \mathrm{d}t \qquad (A.1)$$

where $N(\mu, \sigma)$ is the normal distribution with mean μ and standard deviation σ and $C^{S_{max}}_{S_{min}}(S_K)$ is the uniform distribution in the range $S_{max} - S_{min}$ = Constant, defining the class (8%). As the measurements are performed by the manufacturer and the user, the standard deviation appearing in equation (A.1) would be that resulting from the quadratic combination of the instrumental uncertainties of the manufacturer and the user $\sigma^2 = (\sigma^U)^2 + (\sigma^M)^2$. Integrating equation (A.1):

$$p(S_K) = \frac{Erf\left[\frac{S_K - S_{min}}{\sqrt{2}\sigma}\right] - Erf\left[\frac{S_K - S_{max}}{\sqrt{2}\sigma}\right]}{2(S_{max} - S_{min})} \qquad (A.2)$$

where $Erf(x) = \frac{2}{\sqrt{\pi}}\int_0^x e^{-t^2}\,dt$ is the error function.

Santos *et al.* [7] measured the relative difference between the S_K indicated by the manufacturer and their measurements for 364 remaining selectSeed™ from a total of 49 implants, i.e., $(S_{K,i} - S_K^{Ci})/S_K^{Ci}$. In Fig. A.1, the fit of the parameters of equation (A.2) (S_{min} and σ) to these results is shown. $S_{max} - S_{min}$ is fixed to be 8% as indicated by the manufacturer. The systematic deviation between the manufacturer and the user S_K values, $\Delta = (S_{max} + S_{min})/2$, is also presented.

The manufacturer (personal communication of Peter Seyers, Isotron) informs that its instrument is traced at NIST and has an uncertainty of 3% ($k = 2$). Then, the combined standard deviation with the uncertainty of the Santos *et al.* well chamber (4%, $k = 2$) is 2.1% ($k = 1$). The $\sigma = 2.2\% \pm 0.3\%$ ($k = 1$) obtained of the fit to the data of Santos *et al.* is consistent with these values. The systematic deviation between the manufacturer and the user values of S_K resulted in

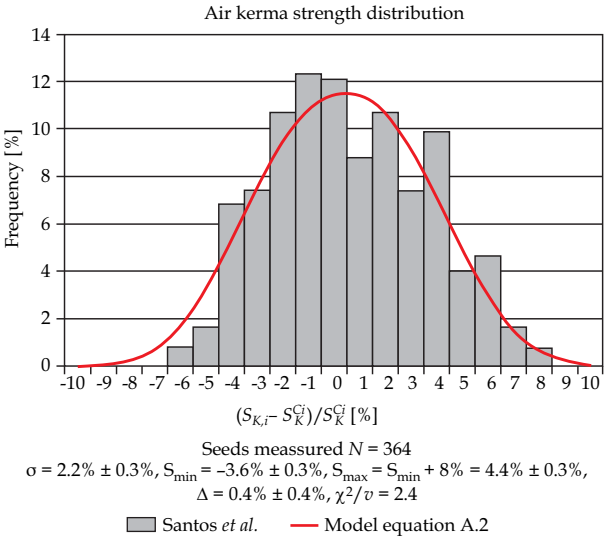

Fig. 5. $(S_{K,i} - S_K^{Ci})/S_K^{Ci}$ results of Santos *et al.* [7] has been fitted to the model of equation (A.2). The model assumes one measurement for both the manufacturer and the user. The standard deviation of the model (A.2) distribution is ∑ = 3.2% obtained by integration. Coverage factor of the uncertainties is k = 1

($\Delta = 0.4\% \pm 0.4\%$ ($k = 1$) that is compatible within uncertainties with no deviation between the user and the manufacturer measurements.

According to these results, we could conclude from the data of Santos *et al.* that the distribution of a given class of seeds follows the model of eq. (A.2) discussed above with a total width of 8%, with respect to the central value of each class with a combined standard deviation of the measurement instruments of σ = 2.2%. The standard deviation of this $p(S_K)$ distribution is ∑ = 3.2%.

S_K distribution assaying 10 seeds with the insert

According to the previous results, we begin assuming that there is not a systematic deviation between the manufacturer and user measurement, ($\Delta = 0$) and that the distribution of a given class of seeds has the form $p(S_K)$ discussed above with a total width of 8% with respect to the central value of the class, with a combined standard deviation of the measurement instruments of 2.2%.

In case in which the manufacturer provides 10 separate seeds, they come from a distribution $p(S_K)$, but with $\sigma = \sigma^M$. The user does a single measurement with the Nucletron insert and she/he measures $\overline{S_K}$. $\overline{S_K}$ should follow a Gaussian distribution (mean and standard deviation Δ_{10} and σ_{10}, respectively) because it is the mean of the S_K of ten seeds. The standard deviation of should be $\sigma_{10}\sqrt{\frac{\sum^2}{10} + \left(\sigma^U_{Nucletron}\right)^2}$

where ∑ is the standard deviation of $p(S_K)$, but with $\sigma = \sigma^M$ and $\sigma_{Nucletron}$ is the uncertainty associated to a measurement with the Nucletron insert.

Acknowledgements

This study was supported in part by Generalitat Valenciana (Project PROMETEO2008/114), FEDER, Ministerio de Ciencia e Innovación, Spain (Project No. FIS2010-17007) and by a research agreement with Nucletron B.V. Veenendaal, The Netherlands.

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