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FULL PAPER

Comparison of Axxent-Xoft, ^{192}Ir and ^{60}Co high-dose-rate brachytherapy sources for image-guided brachytherapy treatment planning for cervical cancer

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Objective: To evaluate the dosimetric differences and similarities between treatment plans generated with Axxent-Xoft electronic brachytherapy source (Xoft-EBS), ^{192}Ir and ^{60}Co for tandem and ovoids (T&O) applicators.

Methods: In this retrospective study, we replanned 10 patients previously treated with ^{192}Ir high-dose-rate brachytherapy. Prescription was 7 Gy $\times$ 4 fractions to Point A. For each original plan, we created two additional plans with Xoft-EBS and ^{60}Co . The dose to each organ at risk (OAR) was evaluated in terms of $V_{35\%}$ and $V_{50\%}$, the percentage volume receiving 35% and 50% of the prescription dose, respectively, and $D_{2\text{cc}}$, highest dose to a 2 cm³ volume of an OAR.

Results: There was no difference between plans generated by ^{192}Ir and ^{60}Co , but the plans generated using

Xoft-EBS showed a reduction of up to 50% in $V_{35\%}$, $V_{50\%}$ and $D_{2\text{cc}}$. The volumes of the 200% and 150% isodose lines, however, were 74% and 34% greater than the comparable volumes generated with the ^{192}Ir source. Point B dose was on average only 16% of the Point A dose for plans generated with Xoft-EBS compared with 30% for plans generated with ^{192}Ir or ^{60}Co .

Conclusion: The Xoft-EBS can potentially replace either ^{192}Ir or ^{60}Co in T&O treatments. Xoft-EBS offers either better sparing of the OARs compared with ^{192}Ir or ^{60}Co or at least similar sparing. Xoft-EBS-generated plans had higher doses within the target volume than ^{192}Ir - or ^{60}Co -generated ones.

Advances in knowledge: This work presents newer knowledge in dosimetric comparison between Xoft-EBS, ^{192}Ir or ^{60}Co sources for T&O implants.

Cervical cancer is the most common cancer for females in the developing world, accounting for over 230,000 deaths per year.¹ In developing countries, most cancers are diagnosed in the later stages, which makes them difficult to treat, and cervical cancer is no exception. According to the American Brachytherapy Society Task Group Report,² cervical cancer with clinical Stages IB2–IVA should be treated primarily with concurrent chemoradiation treatment followed by brachytherapy. Many clinical studies have shown that high-dose-rate (HDR) brachytherapy is of comparable efficacy with low-dose-rate brachytherapy for patients with early- to advanced-stage cervical cancers.^{3,4} Many cancer centres in the developed world have thus adopted HDR brachytherapy treatments for patients with cervical and endometrial cancer.

The main limitation to the widespread adoption of HDR brachytherapy in developing countries is the high cost of the afterloader, and the fact that a new shielded bunker

may need to be constructed if for some reason the afterloader cannot be located in one of the pre-existing teletherapy bunkers. ^{192}Ir has been the radioactive source of choice for most HDR brachytherapy devices, but the ^{192}Ir source needs to be changed at least 3–4 times per year because the half-life of ^{192}Ir is 73.8 days. In a resource-limited setting such as in developing countries, this ongoing cost may be prohibitive. Afterloaders have recently been developed to house the miniaturized ^{60}Co radioactive source, and the use of this source reduces the number of source exchanges from 3–4 times a year to once every 5–7 years owing to its much longer half-life of 5.26 years.^{5,6} This certainly reduces the ongoing cost of source exchanges, but one still needs a shielded bunker to use a ^{60}Co radioactive source.

In the past few years, however, promising new technologies, mainly with electronic brachytherapy systems, have been developed that have eliminated the need for

administering brachytherapy in a shielded bunker. The Axxent-iCad Xofter® electronic brachytherapy system (iCad, Inc., Nashua, NH) is based on a miniaturized 50 kVp X-ray source of 2.2 mm in length. The Bremsstrahlung photon spectrum ranges from 26.7 to 34.5 keV, which is similar to ^{125}I (27.2–35.5 keV; mean, 28.4 keV). The first half-value layer (HVL) of Xofter-electronic brachytherapy source (EBS) ranges from 1.39 to 1.56 mm (Al). The average energy of the Xofter-EBS is about 30 keV, which is <10% of that of ^{192}Ir (380 keV) or ^{60}Co γ -rays (1170 and 1330 keV). The HVL for ^{192}Ir is 2.5 mm of lead while that for ^{60}Co is 11 mm of lead. Because of the low energy of Xofter-EBS, treatments using this source can be delivered in rooms shielded for CT or in regular operating rooms with minimal portable shielding.⁷ This electronic brachytherapy system has been investigated by numerous authors for brachytherapy applications such as accelerated partial breast irradiation, surface treatments for skin cancers and endometrial cancer brachytherapy treatments but not for tandem and ovoids (T&O) applicators.^{7–10} The objective of this study was to evaluate the dosimetry of T&O treatment plans generated using the Axxent-Xofter EBS. These plans were then compared with plans generated with the ^{192}Ir and ^{60}Co HDR radioactive sources.

METHODS AND MATERIALS

All patients treated for cervical cancer in our facility with HDR brachytherapy received an individually customized plan based on the CT scan that was performed after the insertion of the applicator into the patient on the day of treatment. All the patients reported in this series were previously treated in our clinic with an ^{192}Ir HDR source. They all received 25 fractions of 1.8 Gy each in external beam treatment to the whole pelvis followed by three fractions of the same dose to the sidewall as a boost delivered with a midline block. This was then followed by four fractions of T&O HDR brachytherapy of 7 Gy prescribed to Point A. The following organs at risk (OARs) were contoured on the CT scans: rectum, bladder, sigmoid and small bowel. The contours were based on GEC-ESTRO contouring guidelines.¹¹ The CT scan had a slice thickness of 2 mm. The planning objectives were to keep the highest dose to 2 cm³ of the OARs, $D_{2\text{cc}}$, <80% of the prescription dose.

This is a retrospective study in which we created CT-based plans on 10 patients who were previously planned and treated in our facility with T&O applicators using an ^{192}Ir HDR brachytherapy source. Each patient originally had four different

Figure 1. Coronal view of the dose distribution. On the left is ^{192}Ir and on the right the Xofter electronic brachytherapy source. L, left; R, right; F, foot; H, head; P, posterior.

Table 1. Evaluation of volumes of 200%, 150%, 100% and 50% isodose volume for Xofter electronic brachytherapy source-, ^{192}Ir - and ^{60}Co -generated plans for a tandem and ovoids applicator with tandem length of 6 cm

Source type	Volume of 200% isodose line (cm^3)	Volume of 150% isodose line (cm^3)	Volume of 100% isodose line (cm^3)	Volume of 50% isodose line (cm^3)
^{192}Ir	35.6	64.0	125.1	350.4
^{60}Co	36.4	65.1	128.0	356.3
Xofter-EBS	61.9	87.1	134.8	270.2

CT scans and four different treatment plans (one new plan is generated for each fraction of HDR T&O insertion and treatment). For each HDR plan generated with the ^{192}Ir radioactive source, we generated two additional plans using Xofter-EBS and ^{60}Co , for a total of 12 plans per patient. Thus, for this study, we evaluated 120 CT-based plans in total. Treatment planning was performed using the Varian BrachyVisionTM treatment planning system v. 8.9 (Varian[®] Medical Systems, Palo Alto, CA). We had previously commissioned the ^{192}Ir HDR source that we routinely use for our HDR programme. We also had commissioned the Xofter-EBS as well as the BeBigTM ^{60}Co HDR source manufactured by Eckert & Ziegler into the Varian BrachyVision treatment planning system using AAPM-TG43 format for the two sources.^{12–14} For the work reported in this article, we entered the American Association of Physicists in Medicine Task Group 43 data into the planning system and did a hand calculation of the dose predictions at several points for both the ^{60}Co and the Xofter-EBS sources. During the clinical commissioning of the Xofter-EBS source in the planning system, we did extensive measurements in manufacturer supplied phantoms and compared the dose prediction using the radiochromic film. The results were in good agreement and consistent with what has been published in the literature for the Xofter-EBS source.^{7,8} OARs including rectum, bladder, sigmoid and small bowel were all individually contoured. The Foley catheter balloon with the contrast media was also contoured to represent the bladder.

The corresponding data from the three radiation sources (Xofter-EBS, ^{192}Ir and ^{60}Co) are compared in one-way analysis of variance using IBM SPSS[®] Statistics for Windows v. 22 (IBM Corporation, Armonk, NY) at a confidence level of 95%, and an initial p -value was derived. If the initial p -value is >0.05 , it indicates no significant difference between any two data groups. If the initial p -value is <0.05 , further tests between any two groups from the three groups of data are performed using the least significant difference, and p -values will be derived to determine which two groups of data are significantly different in the means.

RESULTS

Figure 1 shows the coronal view of two plans from our database that was generated with the Xofter-EBS and the ^{192}Ir source. We observed that the pear-shaped dose distribution of the prescription isodose line appeared similar for both sources, and we did not discern any obvious significant differences between the two sources in terms of the prescription isodose line. This suggested that sharp dose gradients could be achieved using

a T&O applicator with the appropriate arrangement of sources (or dwell positions) using either of these sources.

Furthermore, Figure 1 also shows that there were significant differences in the 200% isodose (yellow) and 150% isodose lines (pink) between the Xofter-EBS and ^{192}Ir generated plans. For instance, the 150% isodose line for the Xofter-EBS-generated plan is continuous throughout the plane of view and the 200% isodose is mostly continuous. This contrasted sharply with the corresponding lines in the plan generated with the ^{192}Ir source where there are significant breaks in the continuity of both isodose lines (150% and 200%). This finding indicated that near the applicator, the Xofter-EBS created a more extensive “high-dose” volume than that of a comparable plan generated with ^{192}Ir . By contrast, it is not very apparent from Figure 1, but the width of the 50% isodose line (blue) measured through the reference point for the EBS-generated plan is smaller than the 50% isodose width generated with the ^{192}Ir source.

In order to further compare the volumetric dose distribution, we converted the 200%, 150%, 100% and 50% isodose lines into volume structures for three plans using a tandem length of 6.0 cm. All calculated isodose volumes include the applicator volume. The results are displayed in Table 1, which shows the volume of the converted structures with the 200%, 150%, 100% and 50% isodose lines. We again noted from Table 1 that the volume of the 200% isodose line with Xofter-EBS is approximately 74% greater than the comparable volume generated with either ^{192}Ir or ^{60}Co . For the 150% and the 100% isodose lines, these volumes were still about 34% and 7% higher, respectively. However, this trend is reversed for the 50% isodose line where the volume of the isodose line for the Xofter source is only 77% of the isodose volume generated by either ^{192}Ir or ^{60}Co .

Table 2 shows the comparison of the average doses to Point B for the 10 patients in our study. Once again, we saw small differences between the Point B doses for ^{192}Ir and ^{60}Co sources, which averaged about 210 and 203 cGy, respectively. However, the mean Point B dose is only 112 cGy for the Xofter-EBS-generated plans, i.e. about 45% less than the Point B dose for plans generated with either ^{192}Ir or ^{60}Co sources. We summarized from Figure 1 and Tables 1 and 2 that:

- the prescription isodose line appears to be similar regardless of the radioactive source used
- there seems to be no significant differences between plans generated by either ^{192}Ir or ^{60}Co radioactive HDR sources
- there are significant differences in the volumes encompassing the 200%, 150% and 50% isodose lines between Xofter-EBS-generated plans and either of the ^{192}Ir - or ^{60}Co -based plans

Table 2. Comparison of average dose to Point B for Xofter electronic brachytherapy source, ^{192}Ir and ^{60}Co sources with tandem length of 6 cm

Source type	Point B (cGy)	Prescription dose (%)
^{192}Ir	210 ± 27	30
^{60}Co	203 ± 31	29
Xofter-EBS	111 ± 35	16

(d) there are significant differences between the Point B doses for plans with either ^{192}Ir or ^{60}Co and that for plans generated with Xofter-EBS, which is only amounting to about 16% of Point A dose compared with an average of 30% in ^{192}Ir or ^{60}Co plans.

Figure 2 shows the dose distributions in all three orthogonal planes and the dose-volume histogram (DVH) for the bladder, rectum, small bowel and sigmoid for one of our T&O plans. The plans were generated in a standardized fashion with the Xofter-EBS source, ^{192}Ir and ^{60}Co . It seems apparent that the plan generated using the Xofter-EBS source may offer a significant organ dose-sparing advantage especially in the lower dose region since the DVH curve for the ^{192}Ir -generated plan lies above that of the

Xofter-EBS-generated plans for all the OARs. Although this looks intuitive, we quantified the differences by determining the $V_{50\%}$, $V_{35\%}$ and D_{2cc} for the OARs for all the three radiation sources. The D_{2cc} represents a measure of the highest dose to the OARs.

Table 3 shows the D_{2cc} for the rectum and bladder for all the patients in our study; each data point is the average of the values from four different fraction plans. The mean value for all 10 patients would show that there appears to be no significant differences between the values for Xofter-EBS, ^{192}Ir and ^{60}Co , as the p -value is 0.314. For the bladder, the average D_{2cc} was 3.07 Gy for the Xofter-EBS plans compared with approximately 4.11 Gy for ^{192}Ir or ^{60}Co , a reduction of about 25%. A statistical analysis shows that $p = 0.036 < \alpha = 0.05$, concluding that there is a significant

Figure 2. Dose distribution and dose-volume histogram for organs at risk.

Table 3. Evaluation of D_{2cc} (highest dose to a 2-cm³ volume of the organ at risk) for rectum and bladder

Patient	Rectum (Gy)			Bladder (Gy)		
	^{192}Ir	^{60}Co	Xofter	^{192}Ir	^{60}Co	Xofter
1	4.88	5.02	4.76	2.26	2.21	2.42
2	3.48	3.52	2.87	5.28	5.38	4.01
3	4.65	4.93	4.21	3.94	3.99	3.06
4	3.82	3.93	3.21	3.76	3.76	2.39
5	3.77	3.84	3.28	4.67	4.62	3.51
6	3.66	3.70	3.50	3.40	3.11	1.89
7	3.63	3.74	3.09	3.97	3.91	2.80
8	5.07	5.15	4.70	3.51	3.46	2.28
9	5.86	5.91	5.33	5.51	5.53	4.38
10	3.75	4.06	3.42	4.79	5.08	4.02
Average $\pm$ standard deviation	4.26 $\pm$ 0.81	4.38 $\pm$ 0.81	3.84 $\pm$ 0.85	4.11 $\pm$ 0.95	4.10 $\pm$ 1.05	3.07 $\pm$ 0.86
p (three groups) ($\alpha < 0.05$)	0.314			0.036		
$p_{\text{Ir-Xofter}}$ or $p_{\text{Co-Xofter}}$ ($\alpha < 0.05$)	NA	NA	NA	0.024	0.025	NA

difference between the three groups. There are significant differences between Xofter-EBS and ^{192}Ir ($p = 0.024$), and Xofter and ^{60}Co ($p = 0.025$), but not between ^{192}Ir and ^{60}Co ($p > 0.05$, not given in Table 3, which applies also in Tables 4–6) for D_{2cc} to the bladder.

The results for the sigmoid colon and small bowel are displayed in Table 4 for all the sources. There was a small difference for the D_{2cc} for the sigmoid between the Xofter-EBS and ^{192}Ir or ^{60}Co ($p = 0.157$). There was no significant difference for the small bowel doses except that the Xofter-EBS average value was marginally smaller but without statistical significance ($p = 0.865$).

Assessment of the $V_{35\%}$ and $V_{50\%}$ provides a measure of the planned dose in the low-dose regions of the DVH. Table 5 shows the

comparison of the $V_{50\%}$ for the rectum and bladder using all three sources, while Table 6 shows the data for $V_{35\%}$. As shown in Tables 5 and 6, for both rectum and bladder, the normalized volume of tissue receiving 35% and 50% of the prescription dose is smaller for the Xofter-EBS plans compared with plans generated with ^{192}Ir or ^{60}Co (p -values are given to indicate the level of significance).

DISCUSSION

The results obtained in our study, which is based on data from 40 patient plans that were previously generated and treated with the ^{192}Ir HDR source, show that the Xofter EBS can potentially serve as a replacement for ^{192}Ir or ^{60}Co radioactive sources. Similarly, the ^{60}Co source appears to be adequate as an alternative to ^{192}Ir for brachytherapy use in cervical cancer; indeed, it

Table 4. Evaluation of D_{2cc} (highest dose to a 2-cm³ volume of the organ at risk) for sigmoid colon and small bowel

Patient number	Sigmoid			Small bowel		
	^{192}Ir	^{60}Co	Xofter	^{192}Ir	^{60}Co	Xofter
1	2.63	2.62	1.64	1.39	1.42	1.10
2	5.17	5.13	4.51	5.32	5.31	5.14
3	3.09	3.11	2.36	3.76	3.83	3.60
4	4.76	4.76	4.14	6.53	6.55	6.72
5	3.89	3.95	3.12	5.08	5.10	4.65
6	4.89	4.90	4.18	4.61	4.55	4.23
7	4.16	4.12	3.55	3.36	3.31	2.97
8	3.14	3.10	2.56	4.85	4.80	4.40
9	5.03	5.21	4.34	4.39	4.32	3.94
10	3.92	3.72	3.09	3.93	3.61	3.35
Average $\pm$ standard deviation	4.07 $\pm$ 0.90	4.06 $\pm$ 0.93	3.35 $\pm$ 0.96	4.32 $\pm$ 1.37	4.28 $\pm$ 1.38	4.01 $\pm$ 1.47
p (three groups) ($\alpha < 0.05$)	0.157			0.865		

appears to have dose characteristics similar to that of the iridium source. There are, however, a number of caveats that must be taken into consideration by both the Medical Physicist and the Radiation Oncologist during the planning process for Xofter-EBS HDR brachytherapy treatment.

Firstly, lower energy X-rays and γ -rays have a higher relative biological effectiveness (RBE) than higher energy X-rays or γ -rays such as those from ^{192}Ir sources or ^{60}Co .^{15,16} Thus, the “biologically equivalent dose” (BED) around the applicator itself could be exceedingly high and consequently lead to undesirable short- and long-term side effects on the tissues approximated closest to the applicators. One alternative approach to potentially mitigate the BED-related effect on the cervix and endometrium is to use a lower dose per fraction and higher number of fractions when utilizing the Xofter-EBS.

Secondly, the volumes of the 200% and 150% isodose lines are significantly greater when the plan is generated with the Xofter-EBS compared with plans generated with ^{192}Ir or ^{60}Co sources. This means that a larger central volume around the applicator itself is potentially receiving a higher dose and with a higher biological equivalent dose. To minimize toxicity, the midline block that is traditionally used in external beam radiation therapy at doses above about 45 Gy may need to be implemented at a lower external beam dose so as to limit the external beam dose to the

central region of the pelvis. Using a lower dose per fraction and a higher number of fractions for the brachytherapy portion can also help to reduce the BED to levels somewhat more comparable with those generated by ^{192}Ir or ^{60}Co .

Thirdly, Point B, which is located 5 cm lateral of patient midline at the level of Point A in inferior to superior direction, typically receives approximately 25–30% of the prescription dose, representing approximately 7 Gy over the course of traditional HDR brachytherapy. Plans generated with Xofter-EBS only receive about 16% of the Point A dose. Because any attempt to throw the dose more laterally during brachytherapy will likely result in much higher midline doses, an alternative means of achieving adequate dose to Point B may be to supplement it during the external beam portion of the therapy.

Fourthly, we have demonstrated that in this study the Xofter-EBS appears to provide better sparing of the associated pelvic OARs (bladder, rectum, sigmoid and small bowel) than either ^{192}Ir or ^{60}Co sources, generally over the entire dose range as shown in Figure 3, which shows the DVH comparison for a typical implant generated with all three sources. There was only one patient for whom the dose to the small bowel was greater than that seen in plans generated with either ^{192}Ir or ^{60}Co sources. Since the Xofter-EBS has a higher RBE compared with the other two sources, increasing the number of fractions and reducing the fractional

Table 5. Percentage of rectum and bladder receiving 50% of prescription dose ($V_{50\%}$)

Patient number	Rectum ($V_{50\%}$)			Bladder ($V_{50\%}$)		
	^{192}Ir	^{60}Co	Xofter-EBS	^{192}Ir	^{60}Co	Xofter-EBS
1	19.7	20.2	11.9	9.4	8.9	2.1
2	19.7	20.1	11.6	9.6	8.9	11.6
3	61.5	64.9	38.9	77.6	76.6	37.8
4	10.1	16.7	8.7	61.9	67.2	31.6
5	29.1	32.0	20.7	41.9	42.0	18.7
6	10.5	11.3	4.9	33.5	32.1	10.0
7	11.8	13.0	9.3	51.6	48.6	22.7
8	11.6	12.8	5.8	39.4	37.7	17.2
9	13.2	13.7	8.6	87.9	86.6	41.6
10	29.9	30.9	16.8	72.4	70.0	31.5
Average $\pm$ standard deviation	21.7 $\pm$ 15.8	23.5 $\pm$ 16.2	13.7 $\pm$ 10.1	48.5 $\pm$ 27	47.9 $\pm$ 27.1	22.5 $\pm$ 12.9
p (three groups) ($\alpha < 0.05$)	0.280			0.029		
$p_{\text{Ir-Xofter}}$ or $p_{\text{Co-Xofter}}$ ($\alpha < 0.05$)	NA	NA	NA	0.019	0.022	NA

NA, not applicable.

Table 6. Percentage of rectum and bladder receiving 35% of prescription dose ($V_{35\%}$)

Patient number	Rectum			Bladder		
	^{192}Ir	^{60}Co	Xofter	^{192}Ir	^{60}Co	Xofter
1	39.5	41.2	23.1	40.7	38.6	5.9
2	40.9	41.3	23.1	40.6	38.6	6.4
3	86.0	88.0	61.3	99.9	99.5	67.7
4	35.9	43.5	20.6	96.5	97.2	59.6
5	65.3	68.0	48.4	76.6	76.9	42.2
6	39.2	40.1	16.8	74.4	73.2	25.6
7	42.1	43.4	14.1	92.1	90.4	40.2
8	29.0	30.6	14.0	79.0	76.8	38.2
9	37.1	37.2	19.3	100.0	100.0	72.5
10	55.2	55.9	36.3	100.0	100.0	62.9
Average $\pm$ standard deviation	47.0 ± 17.2	48.9 ± 17.2	27.7 ± 15.9	80.0 ± 23.0	79.1 ± 23.7	42.1 ± 24.0
p (three groups) ($\alpha < 0.05$)	0.015			0.001		
$p_{\text{Ir-Xofter}}$ or $p_{\text{Co-Xofter}}$ ($\alpha < 0.05$)	0.016	0.009	NA	0.001	0.002	NA

NA, not applicable.

dose as previously suggested could mitigate the effect of a higher physical dose, if, for some reason, the Xofter-EBS-generated plans increased the dose to any of the OARs of radiation damage. It is also important to note that analysing the data in terms of $D_{0.01\text{cc}}$, $D_{2\text{cc}}$ and $D_{5\text{cc}}$ did not change the conclusions.

CONCLUSIONS

All three sources appear to be suitable for use in cervical cancer HDR brachytherapy, but the use of Xofter-EBS may reduce the doses to the OARs while achieving a comparable dose coverage to the target. The $V_{35\%}$ and $V_{50\%}$ may be useful as indicators of

the quality of the plan as they appear to characterize the lower dose region of the DVH curves more adequately. There were no noticeable differences between the ^{192}Ir and ^{60}Co T&O plans, but the plans generated using the Xofter-EBS offered better sparing of OARs when evaluating the $V_{35\%}$ and $V_{50\%}$, which represent the lower dose in the DVH curve. However, when the $D_{2\text{cc}}$ was used to evaluate the dose to the OARs, there was no significant dose difference in the $D_{2\text{cc}}$ value for the rectum, which represents doses closer to the prescription dose. There was a reduction of up to 50% of the dose between Xofter-EBS and the other two sources when calculating the dose to Point B.

Figure 3. Comparison of dose-volume histogram for a tandem and ovoids implant for plans generated with ^{192}Ir , ^{60}Co and Xofter-EBS sources.

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