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Advances in Treatment of Cancer by Brachytherapy in Kenya, in Particular, Prostate Cancer

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Abstract

Aim: To highlight the developments of treatment of cancer by brachytherapy in Kenya, with particular emphasis on prostate cancer.

Methods and Materials: Currently, different types of cancer can be treated at different institutions. Thyroid cancer was the first brachytherapy treatment by use of I-131 oral solution and now treated with I-131 capsules, reducing the dose burden to the personnel. Other brachytherapy treatments like cervical cancer and esophagus by use of Ir-192 High Dose Rate (HDR) after-loading systems are also available in four institutions. Recent advances of Prostate cancer treatment by LDR I-125 Permanent Seed Implants started at TNH in January/2017 and the relevant patients can now access the service.

Results: We have appreciated increase in the number of prostate cancer patients reaching out for treatment by I-125 Permanent seed implants. When combined with EBRT, the brachytherapy treatment is a boost to better management of the prostate cancer patients. The number of treatment seeds can now be estimated in the pre-planning stage by use of the proposed equation for the Number of Seeds versus the Prostate volume realized for the 36 patients already treated.

Conclusion: Treatment of cancer by brachytherapy here in Kenya started in 1970's and has now developed well in line with the development of the country. In particular, prostate cancer which is the most prevalent male cancer in Kenya, can now be treated by Ultrasound Guided Low Dose-Rate brachytherapy using I-125 Permanent Seed implants. This has tremendously improved the management of prostate cancer patients in this region and the Number of the Seed Implants can now be estimated by use of the proposed equation, y=1.2x+15, relating the Number of Seeds (y) used for treatment and the patient's Prostate Volume (x).

Keywords: Brachytherapy; Prostate cancer; Low Dose-Rate (LDR); High Dose-Rate (HDR); External Beam Radiation Therapy (EBRT)

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Introduction

Treatment of cancer with radiation in Kenya started in the early 1970's when a partnership developed between KNH and Karolinska Institute of Sweden in 1968. Several equipment were donated by the Swedish institution, including one Co-60 radiotherapy machine for external beam radiotherapy (EBRT), one rectilinear scanner for Nuclear Medicine imaging and several QA equipment Two Clinical Radiation Oncologist an a Medical Physicist from Karolinska were part of the program and initially started the Radiotherapy Department at Kenyatta National Hospital (KNH) while training the local radiotherapy staff. In early 1980's, manual cervical cancer brachytherapy treatments were being practiced at KNH, followed by introduction of manual LDR After loader system that used Cs-137 radioactive sources. To-date, four hospitals have HDR brachytherapy equipment for gynecological, esophageal and other related applications, apart from Linacs for EBRT treatments, and treated cancer cases have

continued to rise, as demonstrated by KNH and The Nairobi Hospital (TNH) available data in values shown are in Include this (**Tables 1 and 2**) values shown are in **Figures 1 and 2** respectively.

According to compiled cancer statistics at the TNH, prostate cancer was the most prevalent among male cancers treated in the past by EBRT, **(Table 3)** values are shown in **Figure 3** and ranked second after cervical cancer among both male and female cancers combined. Currently, we don't have a National Cancer Registry, although the Ministry of Health has started the process, but the trend of the cancer statistics at TNH is similar to those from other hospitals here in Kenya [1], and also from other Sub-Saharan African countries [2].

External beam radiotherapy (EBRT) was the only mode of treatment for prostate cancer by radiation since the start of the Oncology & Cancer Treatment Centre at TNH in 2012, until the start of prostate brachytherapy in January/ 2017. The procedure applied is by use of I-125 permanent seed implants in the prostate tumor. Its advantages include a one-time out-patient procedure, continuous low dose-rate irradiation, dose conformity and sparing of normal tissue among others [3]. Clinically localized prostate cancer is managed by radical prostatectomy, brachytherapy, and EBRT. Permanent seed brachytherapy with I-125 implants gets PSA control 10 years higher than that reported for EBRT, and comparable to radical prostatectomy [4-9].

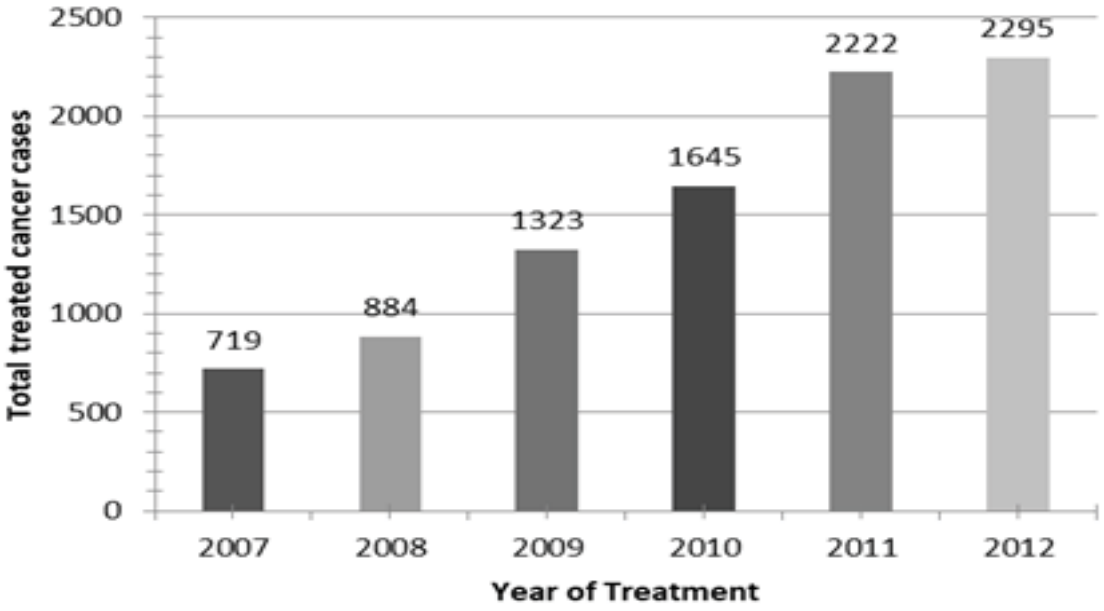

Figure 1 Total cancer cases treated by EBRT at KNH, between 2007 and 2012.

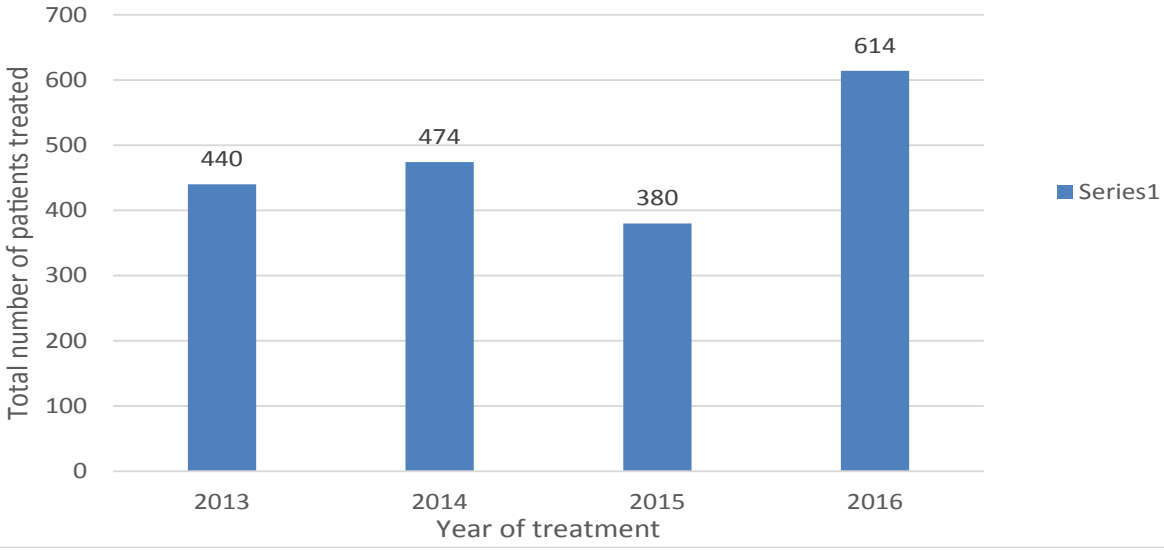

Figure 2 Total cancers patients treated by EBRT at TNH between 2013 and 2016.

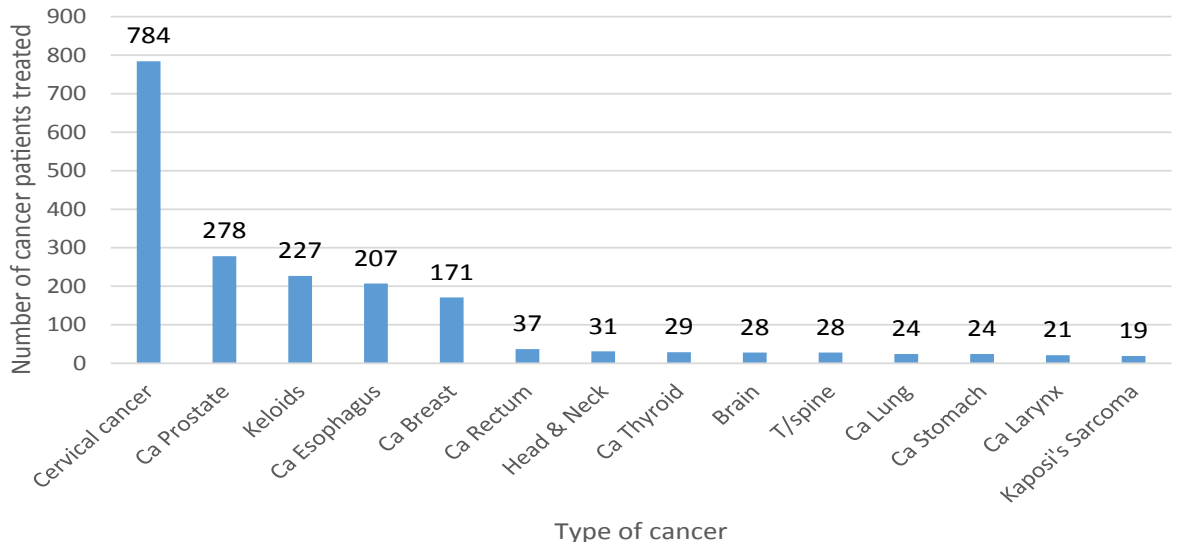

Figure 3 Top 14 common cancers treated by EBRT (Linacs) at TNH between 2013 and 2016.

Materials and Methods

36 prostate cancer patients have now been treated in two years by Ultrasound Guided prostate brachytherapy procedure at TNH. The procedure applied for the treatment is by use of I-125 permanent seed implants in the prostate tumor. Here, prostate brachytherapy is mainly used concurrently with EBRT and may also be used as monotherapy for primary treatment of Low Risk prostate cancer [10].

The American Brachytherapy Society guidelines for ultrasound-guided permanent prostate seed brachytherapy implants have been used. In compliance with Kenya national requirements governing the use and applications, storage and disposal of radioactive materials, strict adherence to the regulatory requirements is normally followed. Proper Licenses for importation of the treatment I-125 Seeds are normally obtained from the National Regulatory Authority (Radiation Protection Board) before importation of the seeds. Only the required amount of seed packs are imported at a particular time for the patients on treatment schedule.

The Ultrasound equipment is a 'BK Medical Flexfocus 400' model, used together with a C-Arm X-Ray Image Intensifier. A Treatment Planning System (TPS) is also available and linked to both the Ultrasound Guidance and the Image Intensifier so that the implant was checked simultaneously with ultrasound and fluoroscopy at the time of the procedure. The prostate brachytherapy team is composed of one Urologist, Radiation/ Clinical Oncologist, 2 Medical Physicists, Anesthetist, 2 Oncology Nurses and a Support Staff. Routine screening of prostate cancer among men is still not practiced in Kenya healthcare facilities [2]. Once a patient is identified as a beneficiary for the treatment, mainly by the patient's PSA levels, Gleason score and other radiological examination findings, engagements start in order to prepare the patient for the treatment procedure in the near future. The patient is normally under general anesthesia during the full procedure.

After the patient and all the equipment have been set, images at separations of 0.5 cm are acquired from the prostate base to the apex. These images now form the basis for the prostate treatment planning. For these 36 patients who were to receive supplementary EBRT dose to the prostate later, the prescribed dose to the prostate volume for the permanent prostate brachytherapy was 110 Gy. The dose prescriptions were based on Risk levels which are dependent on PSA and Gleason levels. The patient's Clinical Tumor classification is also considered during decision of the dose prescription. The process of the treatment planning involves preplanning, intraoperative, interactive and dynamic dose calculation.

During preplanning, sources are carefully inserted at different positions on each image slice and the TPS calculates the combined cumulative dose on the entire prostate treatment area as well as doses to the organs at risk. Depending on the underlying conditions which should not be exceeded for the organs at risk (Urethra and Rectum), an acceptable treatment dose would be arrived at. The Treatment Planning System gives the treatment data, ranging from the prostate dose and volume, Urethra dose and volume as well as the rectal dose. It also generates dose-volume histograms (DVH) and DVH statistics. In particular, we determined how the Prostate Volume varied with the Number of I-125 treatment Seeds.

Results

The treatment data for the 36 patients treated so far was analyzed by their age, PSA level (just before the treatment), Gleason Score, Prostate volume and Prostate Dose, D90% (at Day Zero). Plots of Prostate treatment dose, D90%, PSA levels and Gleason Score were done as on (**Tables 4 and 5**) values are shown in values are

Table 1 Total cancer cases treated by EBRT at KNH, between 2007 and 2012.

Year of Treatment	Total cases treated
2007	719
2008	884
2009	1323
2010	1645
2011	2222
2012	2295

Table 2 Total cancer cases treated by EBRT at TNH, between 2013 and 2016.

Year	Total cases treated
2013	440
2014	474
2015	380
2016	614

Table 3 Top 14 common cancers treated by EBRT at TNH between 2013 -2016.

Type of cancer	Treated cases
Cancer of the Cervix	2877
Cancer of the Breast	2228
Cancer of the Esophagus	712
Cancer of the Prostate	563
Cancer of the Stomach	241
Cancer of the Nasopharynx	233
Cancer of the Larynx	216
Cancer of the Thyroid	184
Cancer of the Colon	141
Cancer of the Tongue	137
Cancer of the Rectum	135
Kaposi's Sarcoma	123

Table 4 Day zero prostate dose, D90%, for the 36 patients treated by I-125 permanent seed implants

Patient Number	Prostate Dose, D90%, Gy
1	146.83
2	124.35
3	151.95
4	120.22
5	145.52
6	160.45
7	137.49
8	136.03
9	132.23
10	141.81
11	126.66
12	136.32
13	129.59
14	149.9
15	141.51
16	141.97
17	144.54
18	186.66
19	112.71
20	165.72
21	142.68
22	166.16
23	146.39
24	134.82
25	134.41
26	131.67
27	131.6
28	132.8
29	149.7
30	144.98
31	124.37
32	152.8
33	132.92
34	149.4
35	150.54
36	130.47

shown in **Figures 4, 5A and 5B** respectively. We also analyzed the patients' Prostate volumes and their respective Number of treatment brachytherapy Seed Implants as seen (**Table 6**).

A plot of the Number of I-125 treatment Seeds implanted against the Prostate Volume was compiled (**Tables 6 and 7**) values are shown in **Figure 6**. The graph shows increasing number of implanted seeds with larger prostate volumes. Thus, the number of prostate seed implants was seen to be proportional to the prostate volume and the relationship can be further suggested to be of a linear nature between the two variables. The linear equation for the graph was; y=1.2x+15, where y are the number of I-125 Seeds inserted in the prostate tumor and x the prostate volume. The dose that 90% of the prostate volume received at Day zero (D90%) was analyzed against the respective patient and a plot for 26 patients treated done also (**Table 4**) values are shown in **Figure 4**.

Discussion

The graph of prostate volume against the number of I-125 permanent Seeds implanted for prostate treatment of the 36 patients shows a linear relationship given by the equation, y=1.2x+15. So the larger the prostate volume, the higher is the number of permanent seeds to be applied for the prostate treatment. An estimate of the number of seeds required for treatment of a prostate patient of a certain prostate volume can now be done either by use of the equation or by reference to the graph.

When one or several prostate cancer patients are available, and who require treatment by I-125 permanent seeds brachytherapy implants, proper pre-planning is vital. Planning would require a knowledge of estimates of the total number of seeds for treating each patient, and the number of packs to be ordered for the total patients planned for treatment on the planned date. The pre-planning would help to minimize wastage of I-125 seeds since they are not only expensive but also decay with time if kept for use at later dates.

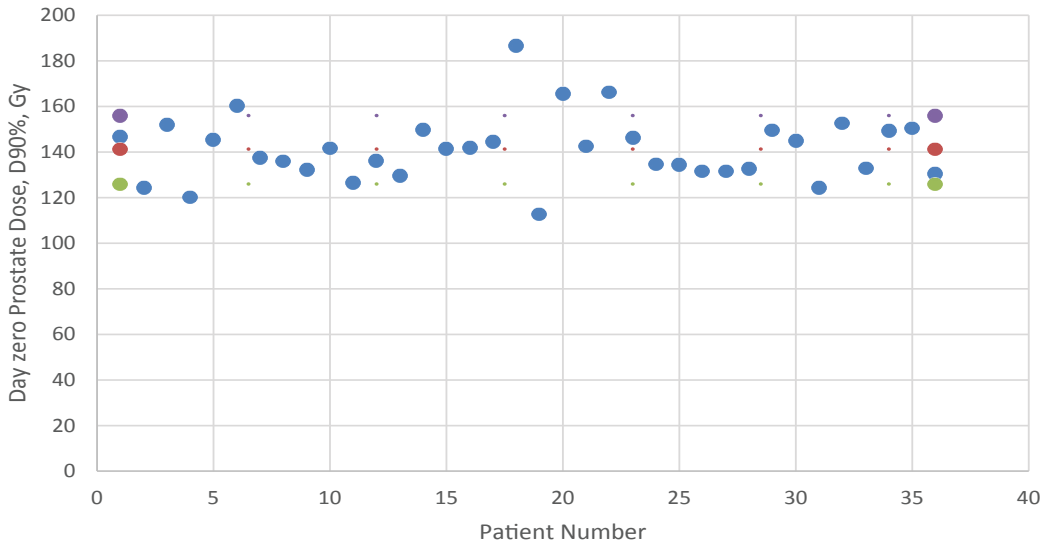

Figure 4 Graph of day zero prostate dose, D90%, for 36 patients treated I-125 permanent seeds prostate brachytherapy.

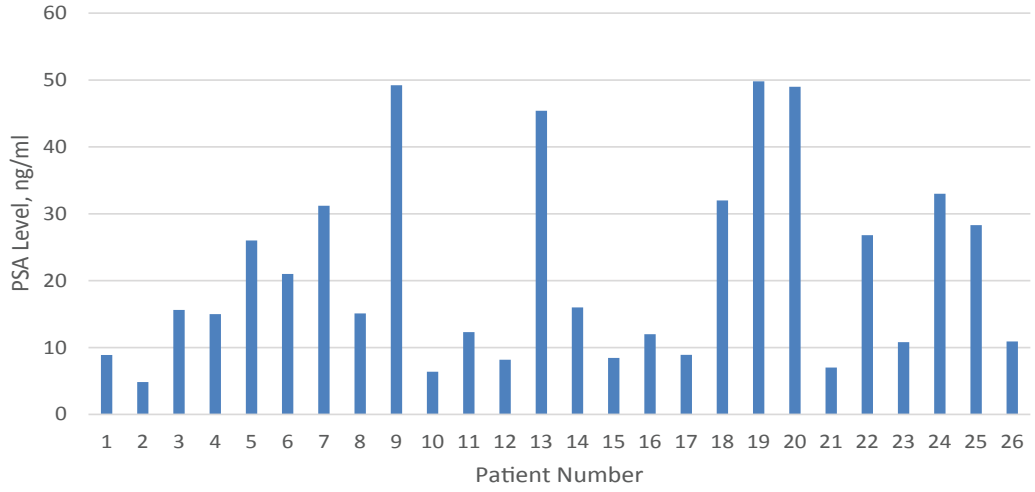

Figure 5a Graph of PSA levels for 26 patients treated by I-125 permanent seed implants.

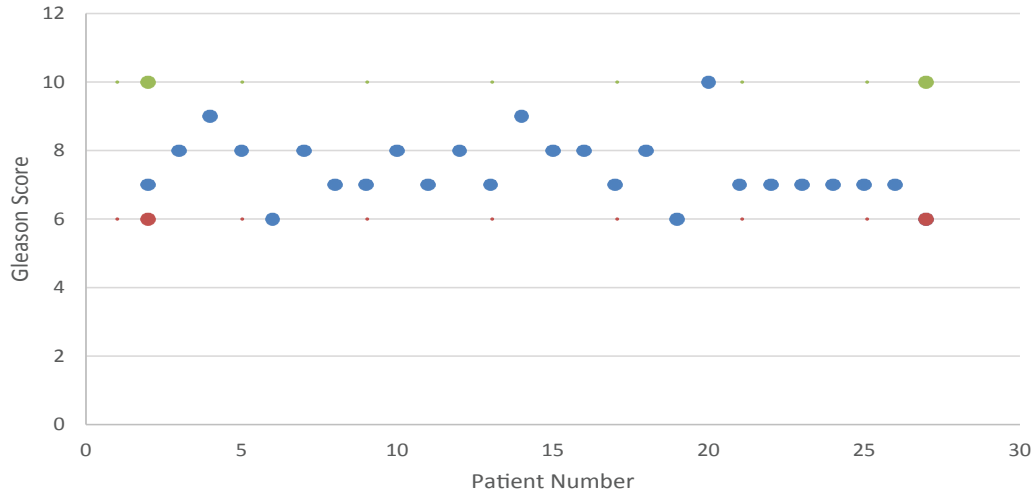

Figure 5b Graph of Gleason score for the 26 patients treated by I-125 permanent seed implants.

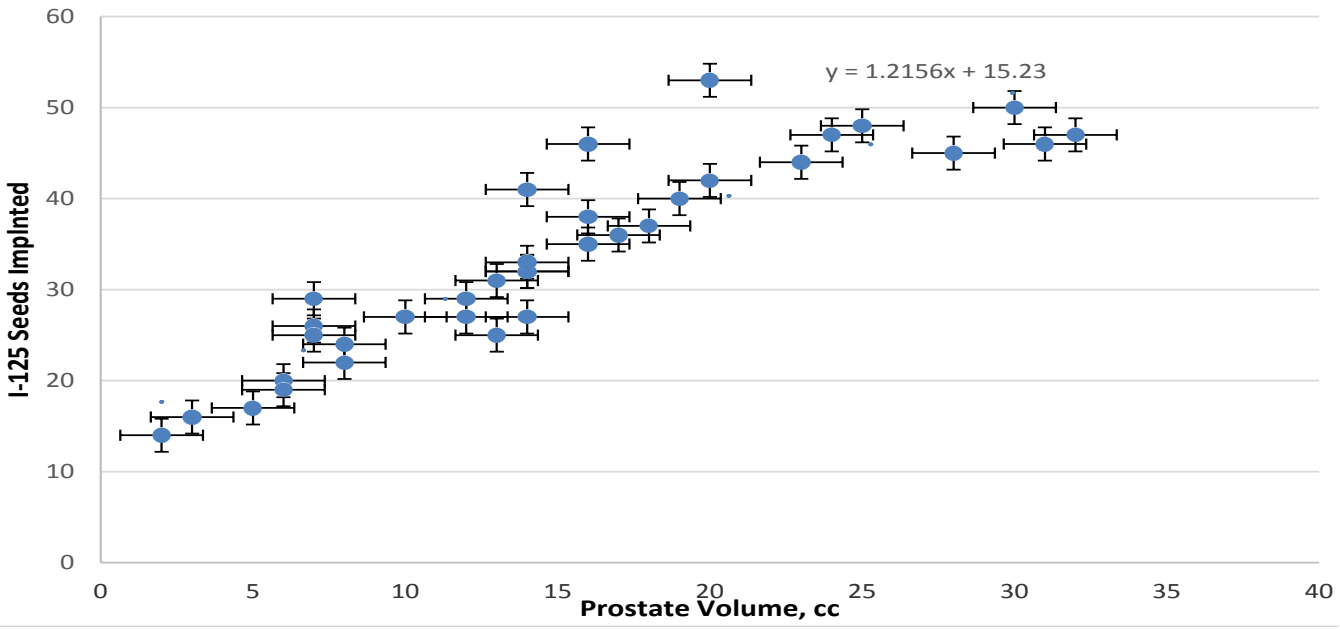

Figure 6 Graph of the number of I-125 seeds implanted on each of the 36 patients treated against the respective prostate volume.

Table 5 Data for age, PSA levels and Gleason scores for 26 of the prostate cancer patients treated by 1-125 seed implants between 2017- 2018.

TNH Number	Age, Yrs	Gleason Score	PSA, ng/ml
1	80	7	8.89
2	50	8	4.83
3	59	9	15.63
4	72	8	15
5	74	6	26
6	64	8	21
7	64	7	31.2
8	63	7	15.1
9	55	8	49.23
10	66	7	6.39
11	63	8	12.3
12	67	7	8.18
13	62	9	45.4
14	70	8	16
15	61	8	8.44
16	61	7	12
17	71	8	8.9
18	72	6	32
19	68	10	49.8
20	72	7	49
21	65	7	7
22	82	7	26.8
23	70	7	10.8
24	63	7	33
25	64	7	28.3
26	56	6	10.9

Table 6 Prostate volume and Number of treatment Seeds used for the 36 patients treated by 1-125 prostate seed implants at TNH in 2017-2018.

Patient Number	Prostate Volume, cc	1-125 Sources used
1	31.65	47
2	6.02	20
3	27.65	45
4	13.76	27
5	7.61	22
6	6.52	26
7	19.71	42
8	14.4	32
9	14.46	32
10	20.48	53
11	11.53	29
12	18.48	37
13	29.67	50
14	16.04	35
15	23.35	44
16	2.98	16
17	14.02	33
18	1.52	14
19	12.5	25
20	15.52	46
21	18.87	40
22	14	41
23	7.91	24
24	24.78	48
25	6.49	19
26	10.25	25

Table 7 Day zero prostate dose, D90%, for the 36 patients treated by I-125 permanent seed implants.

Risk level	Gleason score	Psa level (ng/ml)	Number of patients
Low Risk	≤6	<10	1 (4%)
Intermediate Risk	7	10> and <20	7 (27%)
High Risk	8 to 10	>20	18 (69%)

Conclusion

Since all the patients had a prostate dose prescription of 110 Gy, treatment data for prostate 'day zero' doses (D90%) were analyzed and had a mean dose of 142 ± 15 Gy as shown on the graph in **Figure 4.** Majority of our prostate cancer patients (96%) were classified as Intermediate or High Risk and that's why they would be treated by a combination of EBRT and brachytherapy. The combination of both treatments would tremendously improve the management of prostate cancer patients in this region. The ages for the patients treated by this procedure did not present significant correlation with either the patient's PSA Level or Gleason Score. Treatment of cancer by brachytherapy here in Kenya has now developed well in line with the development of the country. In particular, prostate cancer which is the most prevalent male cancer in Kenya, can now be boosted by Ultrasound Guided Low Dose-Rate brachytherapy treatment using I-125 Permanent Seed implants.

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