First brachytherapy treatment of prostate cancer in Nigeria using low dose rate radioactive iodine 125

Oludare Folajimi Adeyemi1,2,3* and Rachid Mghar4

Abstract

Background: We report the first prostate brachytherapy in Nigeria, using low dose radioactive iodine 125 (I-125) permanent seeds implant.

Case Presentation: The low dose rate brachytherapy using I-125 implants was performed in a private clinic in the city of Benin, Edo state of Nigeria. This pilot study reports the case of the first two patients with prostate cancer. The patients were treated under spinal anesthesia using 2 ml of heavy bupibacaine which is equivalent to 10 mg of bupibacaine. Biopsy, total blood count, electrolytes, urea, creatinine, urinalysis, electrocardiogram, chest X-ray, prostate-specific antigen and bone scan were checked prior to the procedure. The first two prostate cancer patients who were in low risk category successfully received the treatment in the first day of the clinic’s operations. This paper describes the settings in which these clinical operations occurred, detailing the type of technology used, the clinical procedure and the obtained dose distribution.

Conclusions: The paper ends with discussing the overall cost of the investment and the challenges encountered as well as the perspectives of extending the brachytherapy practice to treat other cancer diseases, such as breast and genealogical cancers.

Keywords: Prostate, Cancer, Radioactive, Iodine 125, Low dose, Seed implant, Organs at risk

1 Background

Nigeria is the largest African country with over 206 million population, but faces many health care challenges, especially in the field of cancer treatment due to lack of manpower, underfunding from government, non-affordability of the treatment by the population and the cost of setting up such facilities.

According to the World Health Organization’s (WHO) Globocan project [1], the yearly cancer incidence rate tops 18.1 million cases worldwide. This suggests a rate of 2.4 person affected by the disease for every 1000 persons. At this rate, one expects a total of half million (500,000) cancer cases per year in Nigeria alone. Using the Globocan data, one can further estimate the distribution of this cancer incidence projections per cancer disease site. Figure 1 shows how the half million cases are distributed per type of cancer.

According to the DIRAC database of the International Atomic Energy Agency (IAEA) [2], Nigeria has four (4) LINAC radiotherapy machines available for cancer treatment. This figure sets a load of about 125,000 patients per treatment unit, which is, in the most optimistic scenarios, about 412 times more than the actual capacity of single treatment unit (LINAC) per year [3]. This grim reality sets the country’s capacity to fight cancer as one of the lowest in Africa. Brachytherapy services in Nigeria suffer the same set back, more so that it has only been available for cancer of cervix alone using intracavitary cesium insertion (see Table 1). In the above situation, one must think of a unique strategy that would help the country
solve the problem in the best possible ways; maximizing the cancer treatment efficiency vis-à-vis the success rate. One way to proceed, would be to encourage and provide incentives for private investors to join the cancer fight in Nigeria. The other option will be to consider the selection of technology in a way to optimize the cost of the treatment against the effectiveness.

In this article, we demonstrate that in a private setting and with low budget, one can start-up an oncology clinic which offers radiotherapy treatment in any region of the country. We made a case for prostate cancer, using a low dose rate radioactive Iodine-125 implants, which is a standard for prostate cancer care. Brachytherapy for prostate cancer treatment using radioactive Iodine-125 has been a standard of prostate cancer care for more than a decade and already proven its efficacy in patient survival and quality of life, in addition to its cost effectiveness combined with maximum control of the prostate cancer disease [4–7].

2 Case presentation

2.1 Equipment used for procedure at LA’Newton Oncology Clinic

In August, 30th, 2019, a privately owned clinic, which happens to be the First LDR prostate brachytherapy clinic in Nigeria, opened its doors in Benin City—Nigeria, by treating its first two patients with prostate cancer. The patients received low dose rate Iodine (I-125) implants. The main technology deployed to perform these procedures using Memorial System consists of: (1) a brachytherapy dedicated ultrasound system for prostate cancer; (2) a brachytherapy stand and stepper with grid; (3) an LDR brachytherapy treatment planning system (TPS); (4) Iodine-125 radioactive seeds; (5) a dedicated operation table and operation lights and (6) a hot-laboratory for sterilizing and loading the I-125 implants; (7) a C-ARM x-ray machine for quality control after procedures. Other equipment, such as vital monitors, radiation survey meters and radiation protection jackets, in addition to other consumable products (catheters, sealant, gloves, gowns) are used, as needed, along the procedures (Table 2).

Figure 2 shows the main technology items used for the procedure at the clinic for the LDR Iodine-125 implant. On the top left, is the ultrasound system, Siemens Sonoline G20, on the top right is the operation room, showing operating table and vital monitor (top middle), brachytherapy stand, stepper and probe (top right), on the bottom left, is the C-arm x-ray machine, Philips Pulsera BV 300, and the bottom middle is the sterilizer with hot-laboratory showing loaded brachytherapy needles with I-125 Advantage™ seeds and spacers on the bottom right.

2.2 Realization of the I-125 brachytherapy procedure

The first patient is a 61-year-old man, whose PSA was noticed to be rising gradually following routine annual medical examination 4.9 ng/mL, 6.0 ng/mL, 7.4 ng/mL in succession over 3 years. A digital rectal examination with PSA of 7.4 ng/mL revealed normal prostate, with 1PSS

| Risk group | Clinical stage | PSA | Gleason score |
|------------|----------------|-----|---------------|
| Low (0)    | ≤T2b           | ≤10 | ≤6            |
| Intermediate (1) | >T2b OR >10 OR >6 |       |               |
| High (≥2)  | >T2b AND/OR >10 | AND/OR >6 |               |

Table 1 Current distribution of brachytherapy machine in Nigeria

| Center   | Brachytherapy type | Year of commission | Service type                             | Current status         |
|----------|--------------------|--------------------|------------------------------------------|------------------------|
| 1. ABUTH | LDR                | 1995               | Intracavitary for cancer of cervix only  | Not functioning        |
| 2. UCHI  | LDR and HDR        | 1987 and 2007, respectively | Intracavitary for cancer of cervix only | Not functioning        |
| 3. LUTH  | LDR                | 1975               | Intracavitary for cancer of cervix only  | Not functioning        |
| 4. NHA   | LDR                | 2000               | Intracavitary for cancer of cervix only  | Not functioning        |
| 5. FMCG  | LDR                | 2010               | Intracavitary for cancer of cervix only  | Functioning            |
| 6. LNOC  | LDR                | 2019               | Prostate and breast implant for cancer of prostate and breast, respectively | Functioning            |

Fig. 1 Estimated distribution of cancer incidence, per tumor sites, in Nigeria

Table 2 A commonly used risk group stratification scheme

| Risk group | Clinical stage | PSA | Gleason score |
|------------|----------------|-----|---------------|
| Low (0)    | ≤T2b           | ≤10 | ≤6            |
| Intermediate (1) | >T2b OR >10 OR >6 |       |               |
| High (≥2)  | >T2b AND/OR >10 | AND/OR >6 |               |
score of 4. The MRI of the prostate (unfortunately done after biopsy) showed a prostate measured 42 mm AP by 50 mm transverse by 42 mm craniocaudal in size for a calculated volume of 44 cm$^3$. The post-biopsy hemorrhage limits evaluation for focal prostate carcinoma. No definitive focal suspicious signal abnormality identified in the prostate gland. Adenopathy is negative. PI-RADS category: known cancer.

The report of biopsy indicates prostatic adenocarcinoma Gleason score $3 + 3 = 6$. This classified the patient as low risk based on the clinical staging T1 No Mo Gleason score of 6 and PSA of 7.4 ng/mL. The results of total blood count, electrolytes, urea, creatinine, urinalysis, electrocardiogram, chest X-ray and bone scan were all normal. The second patient is a 55-year-old known hypertensive patient who presented with three (3) months history of difficulty to start or stop urine flow. Digital rectal examination (DRE) query induration in the left lobe. PSA was 15 ng/mL. The MRI reported a normal size prostate with no discrete focal malignancy demonstrated. Biopsy report revealed adenocarcinoma of the prostate gland, with a Gleason score of $3 + 4 = 7$, ISUP grade 2. The report of bone scan was normal. The patient was also classified as low risk based on the staging, Gleason score and PSA.

Based on the preliminary prostate volume study for each patient, the amount of radioactive I-125 seeds needed for the brachytherapy treatment were calculated, and then ordered from the USA. The model of the seeds selected for the procedure were I-125 Advantage™.
[8, 9] from ISOAID which is a premier medical device company that manufactures and markets brachytherapy products. The seeds were shipped at an average activity timed to reach 0.4 mCi (0.508 U) per seed once arrived at the clinic in Benin City—Nigeria. At the Clinic, the seeds were sterilized then loaded into sterile brachytherapy 18-gauge needles, biologically inert spacers are used to separate the radioactive seeds inside the needles and help the control of placing each seed into its specific location accordingly with the specific personalized treatment plan of each patient.

The two patients were treated under spinal anesthesia using 2 ml of heavy bupibacaine which is equivalent to 10 mg of bupibacaine. The choice of the anesthesia type was driven by the patients’ choice, who preferred to stay awake during the procedure.

Figure 3 is a picture showing the consultant performing the procedure of seeds implants on patient 1. Figure 4 on the top left shows the seeds placement within the prostate gland, on the top right, the final dose distribution (isodoses), and on the bottom, the dose volume histograms (DVH) for the prostate and organs at risk, namely the bladder and the rectum. The two procedures were successfully completed within an hour each without any complications. The total seed used for these two patients were, respectively, 80 and 60 seeds.

After the completion of the procedure, the two patients were moved to the recovery room for observation and were later discharged after about 4 hours; based on the fact that the patients were fully conscious, awake, active and able to walk to the rest room to make urine voluntarily. The patients were accompanied with members of their families before and after the procedures.

The patients were given a 1-week appointment as a form of short visit to detect any side effect that will need immediate physician attention. At 3 months, the patients were also seen for second visit. The first PSA and bladder assessment including sexual functions, were assessed during this visit. A similar visit was scheduled for 6-month, 1 year, and then every 6 months.

Cancer can be curable when the patient presents early, but once it is advanced the chances of cure is slim. We have got to educate the public to get over the stigma of the disease, seek treatment and not to be shy about it [10]. Prostate cancer is typically a disease that is ignored at the early stage most especially when it is asymptomatic and most men may not present early either for lack of awareness or they see it as a form of social embarrassment, which is often detrimental to their health and quality of life [11, 12].

Overall, the experience of this first pilot venture of privately operating a brachytherapy facility in Nigeria is very encouraging and incite on duplicating such project in other regions and cities of the country. Though, the process of acquiring the various certifications and authorizations required to launch and operate the facility has been challenging and at time intimidating, persistence and hard work, help overcoming all these challenges. In the flip side, it is an undertaking that is much rewarding when cancer patients can access the care, receive the treatment and benefit from it.

The total cost to establish the facility was approximately Seven Hundred and Forty-Eight Thousand US Dollars ($748,000USD), which was funded by the clinic. The AROI partners provided support for the purchase, supply, installation and maintenance of all the medical devices in the clinic, in addition to training of manpower like the radiation oncologist, the physicist, nurses and other supporting staff.

The facility has offered scholarship in form of clinical rotation for junior and senior residents from other institutions who may be interested in learning the skill. The clinic through AROI has also trained a physicist and technician from other institutions. The goal is to build human capacity and to ensure that radioactive seed implants are replicated in all the other five geopolitical regions of Nigeria. The clinic is in the last stage of securing National Health Insurance Scheme, so that the treatment can be available for low income earners and grassroot population.
On the cost of the facility, while it is not cheap, it is within reach, especially, if one finds the right partner to team up with. There is the need for a partner who is armed with adequate experience and share the same vision and motivations to help solve the cancer problem in the region. In our case, we largely benefited from our American partners, (American Radiology Oncology Solutions (AROS) Inc [13], who possess vast technical and clinical experience. They accompanied our efforts from the beginning, encouraging us along the way not to give up on our goals. The accurate knowledge of the technology, knowing what equipment to select and how to operate is a master key to success.

A comparison cost of this procedure shows that in the USA, it ranges between: $12,000 and $15,000 (State Medicare), $25,000 and $35,000 (Private Practice), in Europe it ranges between $15,000 and $25,000 (France), $12,000 and $19,000 (England), in South Africa and Morocco it ranges between: $12,000 and $15,000; while our private clinic is approximately $7000USD. This is in consideration of the general income of the Nigerian population making the service affordable as much as possible without compromising the financial sustainability of the clinic. In the near future, we intend to extend this same treatment to breast cancer patients and we hope that in midterm, we can qualify our clinic with electronic HDR
technology in order to treat other malignancies, especially the gynecological cancers.

3 Conclusion
Nigerian cancer patients deserve the best treatment options available. There is the need to persevere as a community by working together and discussing ways to create and promote more of these kinds of investments in order to serve our people and take command of resolving our cancer problem.

Abbreviations
AROS: American Radiology Oncology Solutions; ABUTH: Ahmadu Bello University Teaching Hospital; GLOBOCAN: Global Cancer Incidence, Mortality and Prevalence; UCHI: University College Hospital, Ibadan; LUTH: Lagos University Teaching Hospital; NHA: National Hospital Abuja; FMCG: Federal Medical Centre, Gombe; LNOC: LaNewton Oncology Clinic; DIRAC: Directory of Radiotherapy Centres; DNA: deoxyribonucleic acid, DRE: digital rectal examination; DVH: dose volume histogram; HDR: high dose rate; IAEA: International Atomic Energy Agency; I-PS: International Prostate Symptom Score; ISUP: International Society of Urology Pathology; LDR: low dose rate; LINAC(S): linear accelerator(s); MRI: magnetic resonance imaging; PSA: prostate specific antigen; TPS: treatment planning system; WHO: World Health Organization.

Acknowledgements
Dr. Oludare would like to send his thanks to all the people that supported him during the process of opening the clinic, specifically his partners at AROS Inc who supported him all the way and travel to Nigeria to assist me with the first operations. I also would like to thank the Nigerian Nuclear Regulation Authority (NNRA), CCG Sheri Joseph, CC Ku and Mr Okungbowa G. Enasakhare who encouraged me and facilitate the process of opening the clinic.

Authors’ contributions
OFA was the consultant that managed the patients as well as conceived the study and wrote the manuscript; RM is the physicist that did the dosimetry and radiation safety. Both Authors reviewed and accepted the final manuscript.

Funding
None.

Availability of data and material
On Request.

Ethics approval and consent to participate
The study was approved by the review board at LA Newton Oncology Clinic (LNOC/Acad/ethics/01/19), and all participants provided written informed consent prior to study participation.

Consent for publication
The patients gave a written informed consent for publication.

Competing interests
The authors declare that they have no competing interests.

Author details
1 LA’NEWTON Oncology Clinic, Benin City, Nigeria. 2 Department of Radiotherapy and Clinical Oncology, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria. 3 Department of Radiology, University of Benin City, Benin City, Edo State, Nigeria. 4 American Radiology Oncology Solutions, Philadelphia, USA.

Received: 16 January 2020 Accepted: 27 November 2020
Published online: 09 December 2020

References
1. Globocan report, November 2018, WHO, http://gco.iarc.fr/
2. DIRAC data base, IAEA, https://www.iaea.org/resources/databases/dirac
3. Rosenblatt E (2014) Planning national radiotherapy services. Frontiers in Oncology 4:315
4. Fitzpatrick JM (2012) LDR brachytherapy: latest advances in prostate cancer treatment. Br J Urol Int 109(1):13
5. Buegy D, Schneiberg V, Schaefer J, Welzel G, Trojan L, Bolenz C, Wenz F (2018) Quality of life after low-dose rate-brachytherapy for prostate carcinoma—long-term results and literature review on QLQ-C30 and QLQ-PR25 results in published brachytherapy series. Health Qual Life Outcomes 6:21
6. Skowronek J (2017) Current status of brachytherapy in cancer treatment—short overview. J Contemp Brachyther 9(6):581–589
7. Shah C, Lanni TB Jr, Ghielizan M, Gustafson GS, Marvin KS, Ye H, Vicini FA, Martinez AA (2012) Brachytherapy provides comparable outcomes and improved cost-effectiveness in the treatment of low/intermediate prostate cancer. Brachytherapy 11(6):441–445
8. Rivard MJ et al (2007) Supplement to the 2004 update of the AAPM Task Group No. 43 Report. Med Phys 34(6):2187–2205
9. Rivard MJ et al (2017) Supplement 2 for the 2004 update of the AAPM Task Group No. 43 report. joint recommendations by the AAPM and GEC-ESTRO. Med Phys 44(9):297–338
10. Oystacher T, Blasco D, He E, Huang D, Schear R, McGoldrick D, Link B, Yang LH (2018) Understanding stigma as a barrier to accessing cancer treatment in South Africa: implications for public health campaigns. Pan Afr Med J 29:73
11. Ettridge KA, Bowden JA, Chambers SK, Smith DP, Murphy M, Evans SM, Roder D, Miller CL (2018) Prostate cancer is far more hidden: . . . perceptions of stigma, social isolate on and help-seeking among men with prostate cancer. Eur J Cancer Care (Engl) 27(2):e12790
12. Wood A, Barden S, Terk M, Cesaretti J (2019) Prostate cancer: the influence of stigma on quality of life and relationship satisfaction for survivors and their partners. J Psychosoc Oncol 37(3):350–366
13. https://arosmedical.com

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.