



## TECHNIQUES AND PRACTICE OF POST MASTECTOMY RADIOTHERAPY IN NIGERIA: A MULTI-CENTER STUDY

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## **ABSTRACT**

**Background:** Breast cancer affects millions of women worldwide with an increasing incidence in developing countries. Nigeria continues to experience late stage presentation, with as much as 85% of patients presenting with stage III and IV disease. Patients may be at risk of local recurrence after mastectomy due to areas of microscopic residual disease such as the chest wall and regional nodal basins. Post-mastectomy radiotherapy (PMRT) given in adjuvant settings decrease the risk.

**Objective:** To evaluate the practice and techniques of post mastectomy radiotherapy among breast cancer patients treated in Nigeria.

**Methods:** A descriptive retrospective study, used patient data between 2004 and 2015, in all (8) centres in Nigeria. Information was extracted using data proforma.

**Results:** Data of 2143 patients were analysed. All patients received radiation to the chest wall. 39.1% had two regional nodes irradiated, while 38% had only axilla treated, and 6.3% had three regional lymph nodes irradiated. All patients had treatment planning, majority ((93.7%) with conventional technique. The primary beam used was photon with electron boost to the scar (62.8%). Fractionation method was mostly 50Gy in 25 fractions over 5 weeks (61.8%). Three fields were used in treating more than half of the patients (63.0%) while 30.9% were treated with 4 fields' techniques.

**Conclusion:** The study revealed a short fall in access to radiotherapy within the study period. Two dimensional treatment planning method was the dominant with considerable variations across centres in terms of practice and techniques.

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**Key words:** Breast Cancer, Nigeria, Radiotherapy,

## INTRODUCTION

Breast cancer is a disease of global public health concern. It affects millions of women worldwide with an increasing incidence in developing countries. Nigeria continues to experience late stage presentation, with as much as 85% of patients presenting with stage III and IV disease [1, 2]. Several studies indicate that breast cancer in Nigerian patients is often characterised by unfavourable pathologic and prognostic features, such as large tumour sizes (T3 and T4), unfavourable grades, and greater than four axillary lymphadenopathies [3, 4]. Patients may be at risk of local recurrence after mastectomy due to areas of microscopic residual disease such as the chest wall and regional nodal basins. Post-mastectomy radiotherapy (PMRT) is given in the adjuvant setting to decrease the risk of local recurrence by sterilising micro- or macroscopic malignant cells/residual disease [5].

The management of breast cancer requires a multidisciplinary approach, and every patient's treatment is personalised. Treatment modalities include surgery, chemotherapy, radiotherapy, targeted therapy, and hormonal therapy (anti-oestrogen). Since the inception of breast cancer treatment, mastectomy had been the sole standard treatment to achieve local tumour control. This changed about five decades ago; and with the establishment of adjuvant radiotherapy and chemotherapy, the role of mastectomy as single treatment has declined [6]. In most parts of Nigeria, breast cancer patients receive multimodal treatment with mastectomy being the most popular intervention because of the predominance of locally advanced disease at presentation [7].

One of the first breast cancer clinical trials ever performed commenced in 1949. This early trial clearly demonstrated the benefits of PMRT in which it was noted to reduce local relapse rates by 70% with no improvements in overall survival rate [8]. Also established was a high and unacceptable rate of cardiac deaths due to unnecessary radiation dose to the heart. This was attributed to the planning techniques employed at that time [9]. A clear outcome was the need to improve on treatment planning techniques and ensure a reduction in radiation exposure to organs at risk such as the heart and lungs. Radiation Oncologists have heeded this call, and necessary modifications to the treatment planning techniques have been adopted. The results of these early clinical trials have changed practice with reduced cardio-toxicity and maximum benefits recorded [10]. As reported in more recent trials, excess cardiac and breast cancer deaths have indeed reduced [11].

Breast cancer radiotherapy management in Nigeria started in Lagos University Teaching Hospital in 1973, with the acquisition of a Cobalt-60 megavoltage machine. Four decades later, there are eight radiotherapy centres with teletherapy machines in Nigeria. Three of these are Cobalt-60 units located in the University College Hospital, Ibadan; Ahmadu Bello University Teaching Hospital, Zaria; and Eko Hospital, Lagos. The five linear accelerators (LINACs) are at the Lagos University Teaching Hospital, Lagos; University of Nigeria Teaching Hospital, Enugu; University of Benin Teaching Hospital, Benin; National Hospital Abuja, Abuja; and Usmanu Danfodio University Teaching Hospital, Sokoto [12]. To date, thousands of breast cancer patients have been irradiated in all these centres with different techniques.

The radiotherapy treatment planning process is complicated and involves the knowledge of the principles of medical physics, radiobiology, radiation safety, dosimetry, simulation and interaction of radiation with other treatment modalities. Each step in the integrated process of radiotherapy needs quality control and assurance to prevent errors, and ensure that patients will receive the prescribed treatment [13]. Hence, radiotherapy needs to be delivered according to approved international guidelines. These techniques involve multiple steps such as delineation of target volumes and organs at risk (such as the lungs and heart), dose-fractionation scheduling, overall treatment time determination, and so on; all of which should be described and performed in a reproducible manner [13].

In Nigeria, some of the deficiencies in the delivery of radiotherapy services includes; inadequate manpower, protracted machine downtime, lack of maintenance contract, lack of central communication between radiotherapy centres, differences in equipment and personnel amongst centres, and the shortage of radiation therapy resources[14]. This survey, which focuses on the practice and techniques of PMRT given in the adjuvant setting, was conducted to determine the techniques in use across Nigerian radiotherapy treatment centres; and provide evidence to guide the development of radiotherapy treatment protocols. This is essential so that interventions such as a standardised breast cancer radiotherapy guideline can be planned to improve the situation.

## **METHODOLOGY**

### **Patients and study design**

This descriptive retrospective study used patient data between 2004 and 2015, and was carried out in all (8) centres that have megavoltage radiotherapy (linear accelerator and Cobalt-60) machines in Nigeria. The centers are the Lagos University Teaching Hospital (LUTH), Lagos; Eko Hospital (EKO), Lagos; Usman Danfodio University Teaching Hospital (UDUTH), Sokoto; University College Hospital (UCH), Ibadan; National Hospital, Abuja (NHA); University of Nigeria Teaching Hospital (UNTH), Enugu; Ahmadu Bello University Teaching Hospital (ABUTH), Zaria; and University of Benin Teaching Hospital (UBTH), Benin. The study population comprised all histologically confirmed cases of breast cancer who received PMRT to the chest wall and nodal regions at these centres. Patients with deficient clinical information from the treatment cards were excluded.

### **Data collection and analysis**

A data proforma was jointly developed by the radiotherapy departments of the aforementioned study centres. This comprised of questions on radiotherapy treatment planning, and additional data was obtained from patients' radiotherapy treatment cards. Ethical approval was obtained from the institutions Ethical Review Committees. Analysis was done with Epi Info version 7.2, and results presented in frequencies and percentages.

## **RESULTS**

The data of 2143 patients were analysed with variable distribution across the eight study centres as presented in Table 1. The largest proportion of patients came from UCH with 36.6%, followed by LUTH with 14.4%. UDUTH, ABUTH, and NHA had 11.7%, 11.1%, and 10.4% respectively as shown in Table 1.

**Table 1. Patient PMRT distribution across the eight hospitals**

<b>Hospital</b>	<b>Frequency</b>	<b>Percentage</b>
ABUTH	238	11.1%
EKO	179	8.4%
LUTH	308	14.4%
NHA	224	10.4%
UBTH	97	4.5%
UCH	784	36.6%

Hospital	Frequency	Percentage
UDUTH	250	11.7%
UNTH	63	2.9%
<b>Total</b>	<b>2143</b>	<b>100.0%</b>

All patients received radiation to the chest wall with regional node distribution. 39.1% had two regional nodes (axillary and supraclavicular nodes) irradiated, while 38% had only axillary nodal are treated, and 6.3% had three regional lymph nodes (axillary, supraclavicular and parasternal nodes) irradiated. All patients had radiation planning skin marking as presented in Table 2.

**Table 2. Nodal irradiation with skin marks and border point documentation**

	Frequency (n=2143)	Percentage %
Axillary + Supraclavicular nodes	838	39.1
Axillary node only	815	38.0
No node irradiation	356	16.6
Axillary + Supraclavicular + Parasternal nodes	134	6.3
<b>Skin marks</b>	<b>2143</b>	<b>100</b>

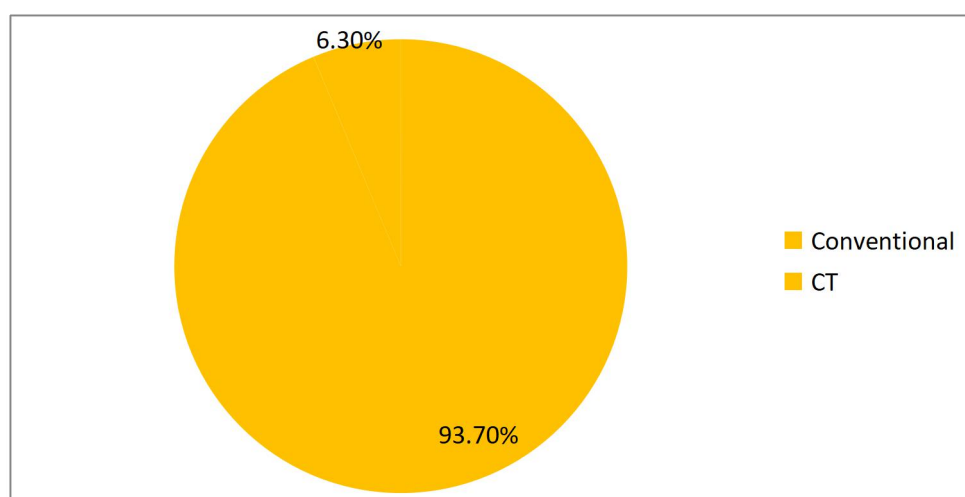
A condensed overview of the treatment planning techniques performed across centres, as shown in Table 3, shows that Cobalt-60 machines were used in three centres (treating 56% of the patients), while five centres used linear accelerators (LINACs) to treat the remaining 44.0% of patients.

**Table 3. Condensed overview of treatment planning techniques**

	No of Radiotherapy Centres n=8	Patient population n=2143(%)
<b>Megavoltage machine type</b>		
Linear accelerator 6MV	5	942 (44)

	No of Radiotherapy Centres	Patient population
	n=8	n=2143(%)
Cobalt 60 1.25 MeV	3	1201 (56)
<b>Planning type</b>		
Conventional 2D planning	8	2008 (93.7)
3D planning	8	135 (6.3)
<b>Beam type</b>		
Photon beam	8	2143 (100.0)
<b>Boost modality beam</b>		
Electrons	3	302 (62.8)
Photons	3	179 (37.2)
<b>Patient positioning</b>		
Supine	8	2143 (100)
Arm abduction	8	2143 (100)
<b>Immobilization device</b>	<b>7</b>	<b>1830 (85)</b>

Conventional 2-dimensional planning was used in 93.7% of cases as against computed tomography (CT), 3-dimensional planning which was used in just 6.3% of cases as depicted in Figure 1.



**Figure 1. Treatment planning methods**

Table 4 shows the type of fields used in the patients. The most used was the 3-field technique (medial tangential, lateral tangential and Direct Anterior SCF field) in 63% of the patients, followed by the 4 field technique (medial tangential, lateral tangential, opposing anterior and posterior SCF field) used in 30.9% of patients..

**Table 4. Distribution of radiotherapy fields**

<b>Field Type</b>	<b>Frequency (n=2143)</b>	<b>Percent</b>
Medial tangential	2143	100%
Lateral tangential	2143	100%
Direct Anterior SCF	1051	49.0%
Ant & posterior SCF	850	39.7%
Parasternal	450	21.0%

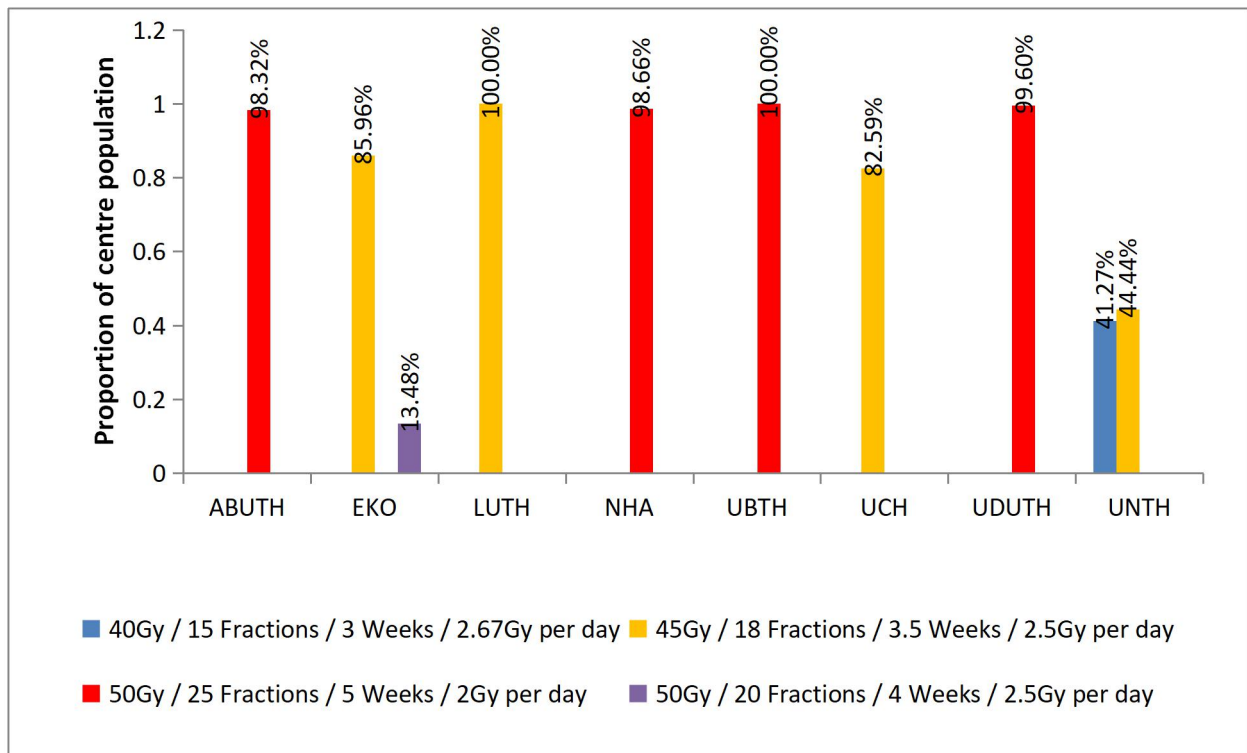
Hypofractionation was practised in four centres – EKO Hospital, LUTH, UCH, and UNTH; while conventional fractionation was favoured by ABUTH, NHA, UBTH, and UDUTH. Based on patient proportions, the predominant fractionation regimen used was hypofractionation in 61.78% while the remaining patients had conventional fractionation regimen as shown in Table 5.

**Table 5: Fractionation regimen**

<b>Fractionation regimen</b>	<b>Frequency (n=2143)</b>	<b>Percent</b>
Conventional fractionation	819	38.2%
Hypofractionation	1324	61.8%
Total	2143	100.0%

The most frequently prescribed dose was 50Gy in 25 fractions over 5 weeks, at a rate of 2Gy per day. This prescription was used across four centers. The remaining centres used 45Gy in 18 fractions in 3.5 weeks at 2.5Gy per day as shown in Figure 2.





**Figure 2: Treatment prescriptions used across centres**

## DISCUSSION

The delivery of radiotherapy involves several steps and various techniques. These are not always in the same order or carried out by the same professionals on a daily basis, and they often include a thorough assessment of the patient, imaging for treatment planning, delineation of target volumes and organs at risk. The treatment plan is then developed and pre-treatment set up, with review and quality control checks carried out by the radiotherapy team comprising the radiation oncologist, therapy radiographer, medical physicist, and others [16].

Nigeria and Egypt bear similarities in the pattern of presentation, with the majority of breast cancer patients presenting with locally advanced disease at diagnosis, and therefore requiring PMRT. However, Egypt has more radiotherapy facilities and better access to radiotherapy [17]. The growth of radiotherapy services in Nigeria has been slow with only eight megavoltage units serving over 155 million Nigerians [18]. This is in contrast to the International Atomic Energy Agency (IAEA) recommendation that there should be one megavoltage equipment per 250,000 population [19]. At the moment, one megavoltage centre serves about 19,000,000

people in Nigeria. This situation is exacerbated by the frequent breakdown of the few megavoltage facilities across the country [20].

Over the study period, 2143 patients received PMRT; a figure lower than expected. The number of irradiated patients is conservatively expected to be half of diagnosed patients. For instance, in 2012, Nigeria recorded an incidence rate of 27,304 new breast cancer cases [22]; yet in the same year, less than 1% of this reported number received PMRT. A study by Kingham et al pointed out that only 10.8% of cancer patients received PMRT in Sub-Saharan Africa [21].

The Philippines, which is also a low and middle income country, provided PMRT to about 20% of breast cancer cases; while in high-income countries such as in North America, access to radiotherapy is about 60% [23].

Probable reasons for this small proportion of patients with access to PMRT in Nigeria include frequent breakdown of machines, lengthy delays in the repair of machines, with some centres rendered inoperable for between six months and 5 years. Some of the existing megavoltage radiotherapy machines are old and hence reduced operating efficiency. Other reasons may be attributed to low awareness of the benefits of radiotherapy amongst health care professionals, high cost of services in a country where majority pay out of pocket, and poor data recording. This scenario is common across Africa, as there is a global shortfall of radiotherapy services, with more than 90% of the population in low-income countries lacking access to radiation services [24]. Nigeria is experiencing a decline in the provision of quality radiotherapy services to the increasing population of cancer patients who require it [12]. However, since Nigeria concluded a successful Democratic Government transition, the Federal Ministry of Health has proposed initiatives to improve existing radiotherapy services and provide seven new radiotherapy machines to different parts of the country [25].

In this study, all patients had PMRT to the chest wall. Ninety three percent of patients received radiation to ipsilateral axillary nodes, 80% to supraclavicular nodes and 21% to the parasternal nodes. This is similar to an Eastern Cooperative Oncology Group (ECOG) trial where radiation was given to the chest wall as well as the supraclavicular, infraclavicular, axillary, and internal mammary nodes [26]. This study reported a high number of regional node basins which is most likely due to the locally advanced presentations of patients. However, it is important to justify the irradiation of certain fields such as the supraclavicular fossa (SCF). Indications for SCF irradiation include large primary tumour size and positive axillary nodal status. There is a 5% risk of SCF recurrence if the level I axillary nodes are

involved, hence level II and III axillary and SCF nodes may be irradiated [4]. This risk quadruples to 20% when there is involvement of  $\geq 4$  axillary nodes, a single node size  $>2$  cm, or involvement of level III nodes; all of which make SCF radiotherapy compulsory [4].

When chest wall target volume delineation is performed, various references and landmarks are used. Approximately 7% of patients were planned with CT planning (Table 3). The use of radiopaque wires to mark out the borders and mastectomy scar for those patients who required a boost was frequent in most centres. Also, there was a wide variation in the treatment field borders used in PMRT and boost planning target volume definition. This is possibly due to varying degrees of knowledge and skill sets of radiotherapy team members, as well as the differing capacities of the megavoltage machines in each centre. Treatment field boundaries were documented in the radiotherapy treatment cards with various boundary references and landmarks. Borders used were commonly marked with ink and the most commonly used field reference points were: superior border – suprasternal notch; inferior border – xiphisternum or 1.5-3cm below the contralateral breast; medial border in the midline or a few centimetres lateral to the midline; lateral border – mid-axillary line (MAL) or few centimetres posterior to the MAL.

Historically, PMRT has been delivered with tangential fields for chest wall and separate fields for regional nodes [27]. In this study, the three-field technique (direct anterior supraclavicular, medial, and lateral tangential fields) was the predominant field type used in 63% of patients. The choice of this field technique may be dependent on ease of setup. The isocentric tangential fields encompassed the chest wall plus or minus the axillary nodes. The third field, a direct anterior supraclavicular field at various depths ranging from 2-3 cm, covers the SCF. Siddon et al [28] used a similar three-field technique but with a different coverage area: two tangential beams and an anterior field that covered the axilla and supraclavicular areas. Benefits of the modified three field method are the simplicity of field set up and the ability to match the field junctions.

The SCF may be treated with two parallel opposed fields, which was received in this study by 30.9% of patients. This results in a four-field technique comprising of opposing anterior and posterior SCF and medial and lateral tangential fields. [29]. The variation in the choice of direct anterior supraclavicular fossa versus opposing anterior and posterior SCF fields in this study may be attributed to the size and depth of supraclavicular lymphadenopathy and dose distribution across this heterogeneous region.

There are five LINACS and three Cobalt-60 megavoltage machines across the eight centres in Nigeria. In this study, 56% patients were treated at a Cobalt-60 center. This is attributable to the fact that the Cobalt-60 machines were operational in Nigeria many years before the first LINAC was commissioned. Also, the LINACS seem to experience unique challenges and long downtimes due to infrastructural, technical and logistic problems; all of which have been experienced since five LINACs were provided to different centres across Nigeria as part of an upgrade in 2003 [30]. Currently, all the megavoltage machines are operating sub-optimally in Nigeria.

The Cobalt-60 is described as being more robust and dependable in developing countries with unstable electricity. In addition to being simpler to operate with the ability to incorporate modern technology such as a multileaf collimator, it is also cheaper to purchase and maintain relative to the LINAC. Although a LINAC poses a lower risk as a radiation hazard, the Cobalt-60 has more dynamic functions and better radiation dosimetry [19]. The IAEA recommends the Cobalt-60 machine for the delivery of radiotherapy in resource-constrained countries like Nigeria [19].

The utilisation of CT planning is sparse as only two centres in Nigeria practised CT planning during the study period. Only 6.3% of patients received CT-planned radiotherapy. This is similar to an old Australian survey that reported that only 3 out of 11 Australian institutions used CT treatment planning [31]. The two centres in Nigeria practising CT treatment planning were able to view the geometry of the target volumes, organs at risk, determine the central lung dose (which did not exceed 2cm), and set up patients and beams to receive homogenous doses. The benefits of CT treatment planning have been reported to include better dose precision, dose homogeneity and patient positioning [31]. The ability to conduct 3-dimensional dose calculations and view the geometric positions of the tumor and healthy tissue on a treatment plan are significant advantages that enable the calculation and optimisation of dose [32]. This results in an increased dose to tumour and reduced dose to normal tissue (therapeutic ratio), thereby reducing radiation-induced complications. This study reveals that 2D planning is the standard planning method used in over 90% of patients. Two-dimensional planning involves delineation of target volume using anatomical references and a conventional X-ray/fluoroscopic simulator where available.

In this study, photon irradiation (the global standard) was used for all patients. Gaffney et al [33] reported the irradiation of chest wall and internal mammary nodes of 140 patients with electron arc therapy to a total dose of 45–50Gy in 5 to 5.5 weeks. In the study, supraclavicular

and axillary nodes were irradiated with two photon fields that were matched. Actuarial 5-year local-regional control (LRC) and disease free survival was found to be 91%, and 64% in the adjuvant group. This substantiates the point that LRC with electron arc therapy of the chest wall is comparable to photon techniques; and with careful attention to treatment planning and dosimetry, electron arc therapy of the chest wall can be safe and efficient [33]. A few other studies have explored the use of high particle beams such as protons. Proton radiation for PMRT is a viable option in a select group of patients. However, it is restricted to clinical trials [34] and facilities for proton therapy are currently not available in Nigeria.

About a quarter of the patients in this study received a boost to the mastectomy scar/chest wall, commonly with electrons (63%) while others received photon boost with the use of appropriate bolus material. The benefits of boost radiotherapy have been established in a large randomized trial, which revealed a significant reduction in local recurrence risk upon the addition of a boost to patients with high risk of recurrence [35].

A critical component of radiotherapy techniques is positioning the patient to ensure reproducibility of the treatment from simulation to the end of therapy, as well as limiting geographical miss [4]. All patients in this study were treated in the supine position, which is commonly prescribed internationally. Similarly, Jabbari et al [29] indicated that patients are usually placed supine on an angled breast board. The role of the breast board is to modify the sternum and chest wall slope. In this study, 78% patients were treated and immobilised with a breast board. There is a role for prone position in whole breast radiotherapy in patients with thick or pendulous breasts [36]. Also, all the patients were placed with the ipsilateral or both arms abducted. However, there were variations in arm positioning – with an arm pole, breast board, or arm abducted with palm behind the head. The abduction of the arm lifts the breast superiorly and thus reduces the dose to the heart; whilst also providing reproducibility of the treatment plan.

Hypofractionation regimen employs a large dose per fraction of 2.2 to 4.0 Gy daily, with a shorter overall treatment period which is usually less than 4 weeks [37]. In this study, 62% of patients were treated with various hypofractionation regimens; the most common regimen being 45 Gy in 18 fractions over 3.5 weeks. The daily dose per fraction size ranged from 2.5 Gy to 3.75 Gy. Also observed was that four centres routinely used hypofractionated regimen while the other four used conventional fractionation prescribed at 50 Gy in 25 fractions. Conventional fractionation is defined as the delivery of small doses of 1.2–3 Gy/fraction on a daily basis over 4–6 weeks [38]. One centre practised both fractionation

regimens equally. The two centres with the highest number of patients predominantly practised hypofractionation which has a shorter treatment time allowing more patient turnover and access to radiotherapy. This is in contrast to a *Zambian* study where 75% of breast and prostate cancer patients were treated with conventional fractionation regimens lasting five weeks [24].

Data from multiple studies showed that hypofractionation and conventional regimens have comparable results in locoregional control and disease-free survival [39]. In the United Kingdom's START-A trial, a dose of 41.6Gy was delivered in 13 fractions over 2.5 weeks in 3.2 daily fractions. A similar Canadian trial employed a regimen of 42.5Gy delivered in 16 fractions over 3.5 weeks. Both studies documented excellent local control and toxicity similar to the conventional schedule of 50Gy in 25 fractions given over 5 weeks, a regimen preferred in the United States of America [40,41].

## **Conclusion**

This study reveals the shortfall in access to radiotherapy in Nigeria between 2004 and 2015 as less than 10% of those with the disease had PMRT assuming an incidence of 27,304 breast cancer cases seen in Nigeria in 2012. This national survey also establishes that two-dimensional planning remains the back bone of radiotherapy delivery to breast cancer patients in Nigeria. Majority of patients received regional lymph node irradiation, which reiterates the prevalent locally-advanced pattern of presentation. In addition, this survey reveals considerable variations in post mastectomy radiotherapy techniques across centres in Nigeria which are wholly or partially attributed to the type of Radiotherapy equipment, patient volume and expertise available at each centre.

## **Recommendations**

On the basis of the findings in this study, it is clear that there is a need to develop a national radiotherapy protocol to ease patient referrals and research; and a federal radiotherapy database registry that records daily practice, techniques, toxicity, outcome and survival of patients receiving radiotherapy. Also, based on the infrastructural challenges being experienced currently, an urgent national radiotherapy task force should be set up to foster a national impact assessment, identify bottlenecks, create sustainable solutions and attract

financial and technological investments in radiotherapy services. There is an obvious need to improve the education and research capacity of radiotherapy professionals, while consolidating the role of quality assurance units.

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