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Research Letter

Investigating the Uptake of Hypofractionation for Breast and Prostate Cancer in Sub-Saharan Africa: A Qualitative Study of Physician and Medical Physicist Perspectives

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Purpose: In prostate and breast cancer, moderate hypofractionation (HF) has demonstrated comparable, if not greater, efficacy than conventional fractionation. There is a stark disparity in the uptake of HF between North America and Africa. Using the Consolidative Framework for Implementation Research, we evaluated barriers and facilitators for implementing HF in Sub-Saharan Africa (SSA).

Methods and Materials: Radiation oncologists and medical physicists working in SSA were recruited via the AORTIC Radiation Oncology Special Interest Group and subsequent snowball sampling. Interviews were conducted virtually between November 2022 and January 2023. Transcripts were analyzed using directed content analysis guided by a Consolidative Framework for Implementation of research interview domains and constructs.

Results: In total, 19 interviewees (17 radiation oncologists and 2 medical physicists) from 11 SSA countries participated, of which 94% noted the use of HF (40.05 Gy/15fx or 42.67 Gy/16fx) in breast cancer clinics and 38% in prostate cancer clinics (60-66 Gy/20fx). While nearly all participants identified the benefits of HF for both clinics and patients, many also noted that the lack of long-term data within an African population created discomfort in using HF. Many participants believed in the utility of HF but expressed a lack of confidence in its use caused by uncertainty about the safety of the technique, especially in centers with cobalt or 3-dimensional conformal radiation therapy-only capabilities. In breast HF, participants expressed concern regarding breast size and ideal eligibility criteria for patients. In prostate HF, on-treatment imaging and lack of fiducials were identified as barriers. Key facilitators in adopting HF included hands-on training, partnerships with disease-site-specific individuals with HF experience, and consensus on patient eligibility and technique requirements.

Conclusions: HF is regarded as a valuable tool for breast and prostate cancer in SSA, and breast HF is widely used. Attention to the use of 3-dimensional conformal radiation therapy with HF, long-term toxicity data in African populations, and training sessions may facilitate further use of HF for prostate cancer.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Introduction

There is a disproportionate burden of mortality and morbidity of cancer in low and middle-income countries (LMICs).[1] In 2012, over half of the 1.7 million women diagnosed with breast cancer were from low-income countries, and the majority of the over 500,000 deaths were recorded in Sub-Saharan Africa (SSA).[2] The International Agency for Research on Cancer estimates that over 57,000 deaths from prostate cancer will occur in 2030, including a 104% increase in the number of prostate cancer deaths in Africa alone.[3,] Treatment for breast and prostate cancer includes radiation therapy (RT); however,[1,4,5] across Africa, only 30 countries are known to have RT machines.[4]

Recent RT guidelines, in taking advantage of radiobiology principles that optimize the therapeutic ratio, have recommended shortened treatment time through the use of a higher dose per fraction (hypofractionation, HF).[6-10] Additional benefits of HF include improved access to RT in lower resource settings by increasing the number of individuals 1 machine can treat and increasing patient convenience while shortening overall treatment time.[5] At baseline, travel times to RT tend to be longer in low-income versus high-income countries.[11]

Clinical trials, mostly conducted in North America or Europe, have shown clinical equivalents between HF and conventional fractionation (CF), predominantly in breast and prostate cancer.[6-10] Yet, the uptake in resource-limited regions has been minimal.[12] This qualitative study sought to assess perceived barriers and facilitators of implementation of HF within SSA and propose solutions, guided by the Consolidated Framework for Implementation Research (CFIR).

Methods and Materials

Study design and participants

This study was deemed exempt by the Johns Hopkins Institutional Review Board. All interview participants provided verbal consent. We identified English-speaking stakeholders in prescribing HF therapy to breast or prostate cancer patients in SSA.

Data collection and analysis

A semistructured interview guide was developed using CFIR, a well-established framework used to evaluate the implementation of health care interventions using multilevel factors.[13] The interview guide investigated as follows: (1) Innovation (HF), (2) Outer Setting (ie, national policies regarding reimbursement or accrual of machines), (3) process (ie, clinical decision-making), (4) inner setting (ie, clinic-specific factors), and (5) individuals (ie, knowledge, training, and awareness). Interviews were conducted between November 2022 and January 2023 using an online platform with audio recording, lasting approximately 30 to 45 minutes. Data collection ended after reaching saturation, established after recurrent themes were noted during interim analysis. Audio recordings were transcribed verbatim and analysis of interview transcripts was completed by authors RKB and SMG via Atlas.ti.[15] The final codebook of 61 independent codes was then applied to a subset of data and modified until interrater reliability approached kappa 0.7. Emerging themes were then categorized according to CFIR domains (Appendix E1).

Results

Participants and clinic characteristics

A total of 19 interviews (17 clinical or radiation oncologists and 2 medical physicists) from 11 countries in SSA (Appendix E2) were completed. In total, 94% of participants noted the use of moderate HF (40.05 Gy/15fx or 42.67 Gy/16fx) in breast cancer clinics and 38% in prostate cancer clinics (60-66 Gy/20fx) (Table 1). All participants identified both breast and prostate cancer as one of the top 3 cancers seen in their clinics.

Quotations from interviews representing each of the subthemes can be found in Table 2.

Domain 1: innovation

1. Eligibility of patients
2. Importance of context-specific data

Physicians noted that the majority of their patients with breast cancer have locally advanced cancer with nodal involvement, a category not traditionally included in early trials for HF. Additionally, physicians noted that a large proportion of patients with prostate cancer in their clinic present with metastatic disease, rendering them ineligible for curative intent radiation and HF. Some participants did offer the possibility of treating oligometastatic disease.[15,16] Barriers to the use of HF expanded beyond patient eligibility criteria of the disease stage to include anatomic considerations of patients (ie, laterality of breast cancer, size of breasts, the weight of patients, and concerns of prostate proximity to the rectum).

An underlying theme across all interviewees was the need for more data from Africa. Clinical trials completed in the Americas or Europe do not have automatic relevance to the African continent, and there was a desire to conduct homegrown research to evaluate how African patients fare with HF. Barriers to accomplishing this

Table 1 Participant demographic characteristics and utilization of hypofractionation

Profession	N = 19	%
Radiation or clinical oncologist	17	89.5%
Medical physicists	2	10.5%
Proportion who completed foreign training	8	50.0%
Current country of work		
Botswana	1	5.3%
Ethiopia	1	5.3%
Ghana	3	15.8%
Kenya	2	10.5%
Madagascar	1	5.3%
Nigeria	3	15.8 %
South Africa	4	21.0 %
Sudan	1	5.3%
Tanzania	1	5.3%
Uganda	1	5.3 %
Zimbabwe	1	5.3%
Current use of moderate hypofractionation in clinic for breast cancer	18	94.7%
Current use of moderate hypofractionation in clinic for prostate cancer	5	35.7 %

included the competing responsibilities of busy clinics and lack of research funding.

Domain 2: inner setting characteristics

1. Machine and technology availability
2. Toxicity concerns

Participants expressed a fear of toxicity that was more prevalent among those who worked in clinics without the availability of modern machines (linear accelerator vs Cobalt), techniques (intensity-modulated radiation therapy, IMRT, and use of image guidance vs 3D conformal RT, 3DCRT), or intensified quality assurance. Participants feared that the use of Cobalt machines or 3DCRT with HF could cause additional toxicity, especially for prostate cancer given proximity to the rectum.[17-19]

Domain 3: outer setting characteristics

1. Patient and referring provider knowledge
2. Regional distribution of knowledge
3. Reimbursements

Interviewees described patient concerns that shorter treatment time meant treatment was not enough or, conversely, that it would result in a worse "burn with radiation." Participants also expressed concern that referring providers were not fully aware of HF, impacting multidisciplinary care. There was a dearth of regional conferences and thus regional distribution of knowledge for HF. In order to combat this, participants recommended homegrown training programs. Participants who worked in areas that ran training programs for radiation therapists, physicists, or oncologists often had a broader utilization of HF.

For participants who worked in the government sector, salary was often fixed, while in the private sector, reimbursement for RT was defined on a per-fraction basis. There was concern that HF would not be implemented in the private sector because of differing reimbursement patterns. Solutions for this were more challenging because participants admitted that each country and health system's insurance and reimbursement process was complex and independent. However, interviewees did underscore the need for policymakers to participate in decision-making and redefine reimbursements.

Domain 4: implementation process

1. Guideline-concordant care in resource-limited settings
2. Mentorship

Participants expressed frustration at the use of guidelines that delineate the use of radiation therapy practices to which they did not have access (ie, requiring motion management). The need for regional-specific guidelines that are concordant with the technology that currently exists in a region was echoed by many participants, expanding on guidelines like the Harmonized Guidelines by the National Comprehensive Cancer Network. Participants also recommended a mentor to guide the execution of HF contours, evaluation of the plan, and determination of dose constraints.

Domain 5: individual characteristics

1. Personal experiences
2. Training

Personal experiences impacted participants' decision to hypofractionate. One participant expressed that the experience of treating a patient who was a colleague's father was particularly impactful. The patient had acute toxicity with rectal bleeding after using HF for prostate cancer and the provider was "disheartened" by the experience, limiting their confidence in using HF.

Participants acknowledged that knowing what to expect with on-treatment and late toxicities with HF and how these differed from CF impacted confidence in using HF. Physicians expressed that this could come in the

Table 2 Subthemes of Interviews and narrative examples organized using Consolidative Framework for Implementation Research (CFIR) domain

CFIR domain	Subthemes of interviews	Narrative examples
Domain 1 Innovation	Eligibility of patients for hypofractionation	Breast cancer "We have big breasts. We were just talking about it today. Africans have a lot of big breasts. There used to be some guidance with the separation of the breasts with conventional hypofractionation. I know with the new fast-forward and forward and all that, I do not see any contraindications in terms of the separation and the size of the breasts. So, we might be a little bit hesitant. And we do not do prone breasts either, so they might be the reasons why." (Participant 6) Prostate cancer "The sad thing is that, I would say, more than 90% to 95% are present to our center, the RT center, with metastatic disease. . . Yes, I would say 90%. When I was a student, we actually had to hunt for patients for whom to treat radically because it was always RT for bone met, spinal cord compression, brain met, or something like that." (Participant 16)
	Importance of context-specific data	"That is very true. I remember actually, one of my senior oncologists. After this journal club meeting, she was like, "Fine. We have talked about hypofractionation, but what is your experience in our population? Unless you give me the experience, I am not going to prescribe it. What is the experience in my advanced Black population?" (Participant 16)
Domain 2 Inner setting	Machine and technology availability	"But our machine, the images and MV imagery (on the treatment imaging system), we do not have the cone-beam CT. For that reason, we have not yet adopted a hypofractionated treatment for prostate cancer. We use conventional treatment most of the time for the few patients we're treating." (Participant 17)
	Immobilization, on-treatment imaging, and motion management availability	Motion management "But I think I went for one of the ESTRO meetings somewhere in Vienna, and the presentation was something about breasts, and it was breath hold techniques. And then during my observership at MD Anderson, there was also one technique that they actually used for—for lung. So breath holds, and then they admit the radiation when the tumor was in a certain phase or some complicated something. Then I was like, Oh, this is something I can not translate into my clinic. So once it is something that is not too doable and certain, then I really do not go chasing it. Otherwise, then the toxicity to the patient maybe will far outweigh the benefits. . ." Use of fiducials for prostate cancer—motion management "For example, moving to ultrahypofractionation is not something that is actually feasible at the moment because of our The fact is, we do not have MRI scans available. We do have it available, but it is not easily accessible. And we also do not have simple things like fiducial markers. Our image verification at the moment is limited to just a cone-beam CT scan, so to be able to institute a treatment like ultrahypofractionation for prostate becomes very difficult to do without those things. And also, the training of staff; people are not trained to do these kinds of treatments. Although it is recommended and is an option, it is not something that can be instituted at the moment." (Participant 14)
Domain 3 Outer setting	Patient and referring provider knowledge	"I think the main misconception among our patients is that they do not really have an idea about these 25, 5, or 15 treatments. They still have the idea, however, that you are going to burn with radiation, and if you do it in a shorter period of time, is it not going to be worse? That is definitely a concept that is among the patients or even the nursing staff who are not trained well. That is the one thing I have come across—that patients are still quite scared. They are not well educated. They have had experiences of other patients, perhaps years ago, and they still hold that picture in their heads." (Participant 12)

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Table 2 (*Continued*)

CFIR domain	Subthemes of interviews	Narrative examples
	Policies on machine buying and maintenance	"(The linear accelerator) It is down since installation. It never treated a single patient. . . The reason is because when our institute bought the machine, it is during the US sanctions against Sudan. So, we could not base this machine directly from the. . .company. So, it is both from third party and then because of the sanction, we could not get some of the equipment, spare parts took time, then that is just going on. So, this machine never treated a single patient. Now the machine is getting old. Even like 2 to 3 years ago, the. . . company came and tried to solve the machine's problem, but it does not work. . . Nobody knows now what will be done. There is no clear plan. Before your call, I was discussing with our Dean of the Institute. He asked about what will be the plan of this machine because it is not working. We need space." (Participant 9)
	Regional distribution of knowledge	"In terms of our hospital protocol, we have made—people do require permission from the hospital to get our protocols, but it is something that we share with other teaching hospitals, as well as other institutions outside of South Africa. We ourselves run our own training program called Access to Care to try and improve RT in Africa in general. And prostate and breast are big, big modules where we have teams that consist of an RO, a physicist, and an RTT that actually join for these courses, where we teach them what we do here. . . And so most of our protocols do get shared through that platform. And also, it is trying to empower people to develop their own protocols for their institution that would work in the environment and the resources that they have. So yes, it is shared, especially with people that have similar setups in terms of infrastructure, et cetera." (Participant 14)
	Reimbursements	"Because we are in a public setting, so it does not matter. There is no reimbursement for the physician. But if the patient is being treated privately, then obviously the reimbursement to the physician will be lower. And the government—the insurance—what can I say? The insurance, if it is the public one, the National Hospital Insurance Fund does pay the doctors for doing RT. No. They only pay for the sessions and for the planning. If it is in the private setting, then the physician has to negotiate with the hospital for a percentage. Obviously, if it is 20% or 30% of what the insurance reimburses, then as a physician you only get that fraction. So the more the fractions, obviously, the better the reimbursement if it is in the private setting. But in the public setting, it does not matter." (Participant 2)
Domain 4 Implementation process	Guideline-concordant care in resource-limited settings	"You would need to use older guidelines because when you use newer guidelines, you are finding that. For example, if you use ASTRO, they are talking of SBRT for lung mass. You do not even know what SBRT is, so you go a bit backward and use the older guidelines, which are more tailored to what you have. Even with chemotherapy, it is the same thing. They are saying, "Give pertuzumab first-line for HER2-positive," and you are like, "I do not have pertuzumab, so I am going back to before pertuzumab." So we are behind in that." (Participant 13)
	Mentorship	"Because sometimes I like to get in touch with someone who's doing prostate. And then I can be having a lot of discussions with the person, and then I can see if I can do more of the hypofractionation in prostate." (Participant 11)
Domain 5 Individual characteristics	Personal experiences	"Yes. Because the biggest catch is that rectum, and it is very sad when patients keep coming back with rectum bleeding. When I came back from South Africa, I was very enthusiastic about hypofractionation, but only one patient taught me a lesson. He was a father to a colleague of mine, a doctor, and he had prostate cancer. And he did not want radiation for the prostate, but I convinced my friend. I told her, "No, your dad needs RT." And we put this guy to hypofractionated radio in 30 Gray in 15, and he started rectal bleeding. I was so disheartened. From that time on, I only choose wisely which patients I will hypofractionate. Sometimes as much as you have data, but just 1 patient may change your practice. You have to audit yourself. "Is it I did a mistake or what? But with more and more data and more and more patients getting onto hypofractionation, and if we can see the reaction is not that bad, I am sure people will change their practice and adapt to it." (Participant 2)

(*continued on next page*)

Table 2 (*Continued*)

CFIR domain	Subthemes of interviews	Narrative examples
	Training	"I would like to learn more and teach more on the benefits and advantages of hypofractionation in certain clinical cases. And then I would also like to make sure we are treating what we have planned. I would like to improve our imaging on-treatment. What else? And maybe gain experience by way of carrying out studies so that we actually learn more about hypofractionation in our patient population. I think those will be the 3 major things." (Participant 16)

Abbreviations: CT = computed tomography; ESTRO = The European Society for Radiotherapy and Oncology; HER2 = human epidermal growth factor receptor 2; MV = megavoltage; RO = radiation oncologist; RT = radiation therapy; RTT = radiation therapist; SBRT = stereotactic body radiation therapy.

form of hands-on training for physicians and physicists, as well as nurses and radiation therapists.

Discussion

To our knowledge, this is the first qualitative study to identify and prioritize interventions to increase the use of HF across Africa (Figs 1 and 2).

The largest international survey conducted on HF practices was conducted in coordination with the European Society of Radiation Oncology with over 2000 radiation oncologists. Their results highlight a stark disparity in uptake: utilization for HF in prostate cancer was highest in North America (94.3% for low-risk prostate cancer) but lowest in Africa (18.8% for low-risk disease). For breast cancer, following a node-negative lumpectomy, 97% of respondents in North America used HF, but only 40% of respondents in Africa used HF. This disparity was explained in part by barriers including concern for late (30.6%) and acute toxicity (29.2%) from aggregate survey data.[12]

Our results indicate a similar pattern, whereby only 35.7% of participants used moderate HF in their clinics for prostate cancer. However, the uptake for moderate HF for breast cancer was more pronounced, at 94.7%. The difference in these disease sites can be partly explained by radiation technique. HF for breast cancer readily uses 3DCRT, which is more widely available on the African continent than IMRT. Further, the prevalence of localized breast cancer is higher than that of prostate cancer, negating the utility of curative HF. Participants highlighted priority areas for focusing on interventions to increase access and utilization of HF, summarized in Fig. 1 (1 prostate cancer and 2 breast cancer), and described below.

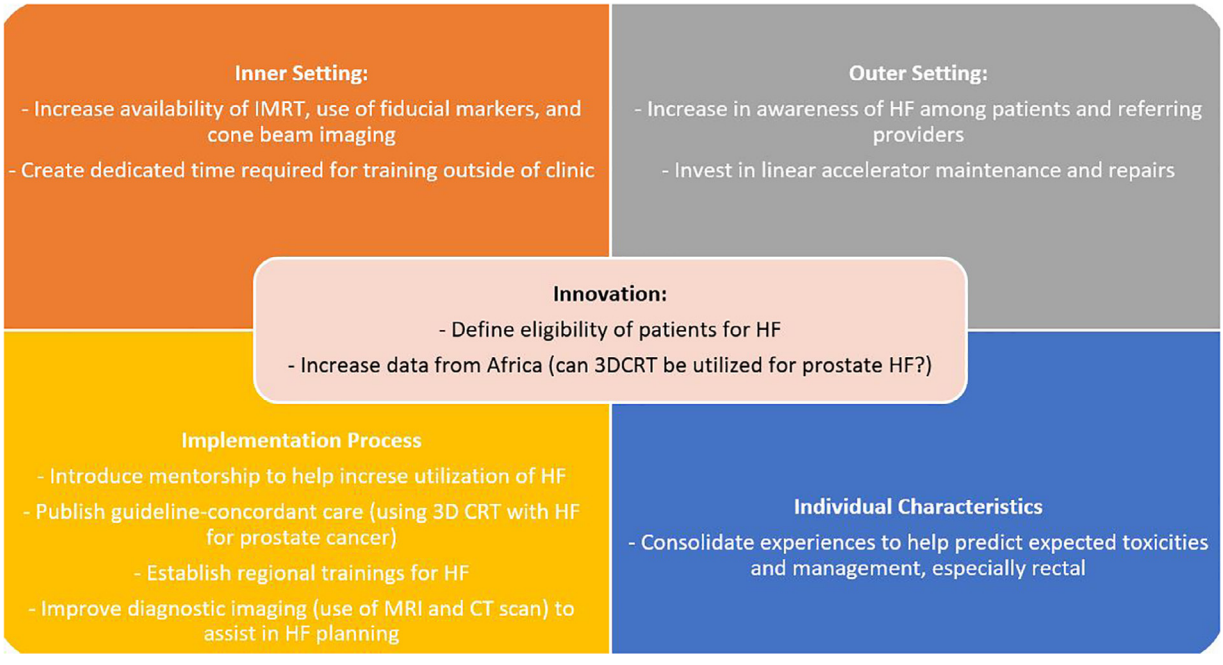

Figure 1 Specific recommendations for increasing utilization of prostate cancer hypofractionation based on CFIR Analysis.
Abbreviations: CFIR = Consolidative Framework for Implementation Research.

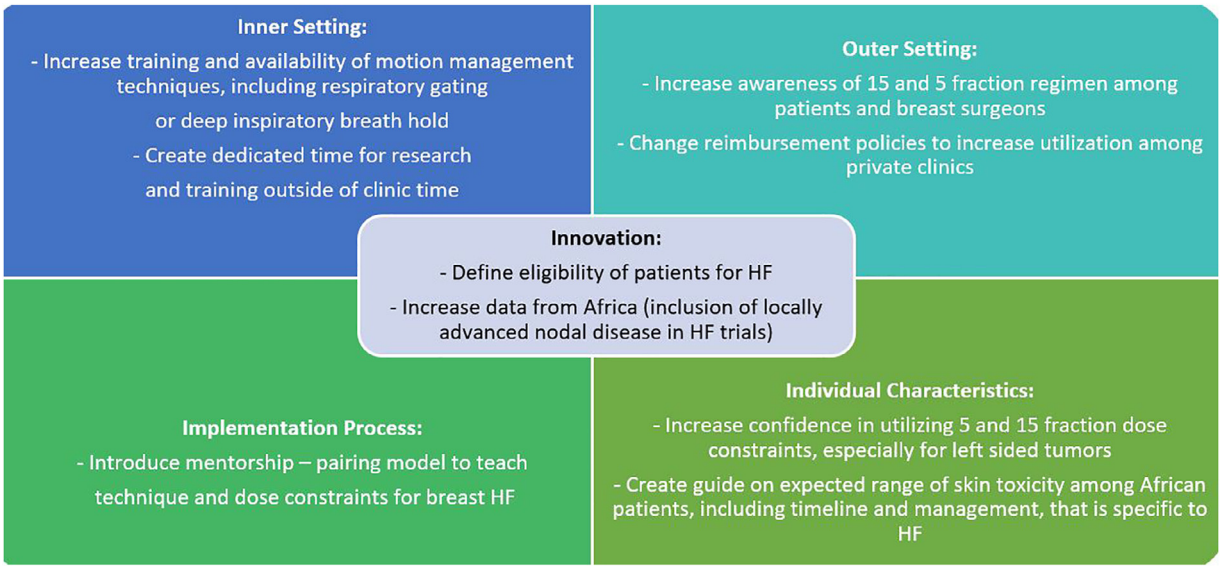

Figure 2 Specific recommendations for increasing utilization of breast cancer hypofractionation based on CFIR analysis.
Abbreviations: CFIR = Consolidative Framework for Implementation Research.

Challenges and proposed solutions

At the level of innovation (domain 1), participants expressed a desire for clear criteria for eligible patients for HF. Characteristics needed included cancer stage, nodal status, and anatomy of the patient (ie, body mass index and size of breasts).[20] Participants also expressed a desire for more data on technique, constraints, and toxicities in the African context. There is a documented dearth of data, specifically in randomized controlled trials (RCTs), published from LMICs. Dodkins et al previously identified phase 3 RCTs between 2014 and 2017 and noted that 77% of the RCTs were performed in high-income countries and only 8 RCTs (13%) in a single LMIC.[21] Potential explanations for this include the conflicting responsibilities of busy clinics with understaffing that limits the ability of physicians to conduct and publish research and limited funding opportunities. In a recent publication, Dee et al[14] identified the political and industrial interests that can influence research and emphasized the need for collaboration. This is especially true when discussing radiation trials, as oncology research can be primarily fueled by pharmaceutical companies and medical oncology advances.

Focusing on personnel recruitment and retention while simultaneously increasing funding specific to African investigators is critical. For example, the Beginner Investigator Grant for Catalytic Research (BIG Cat) Initiative by the National Cancer Institute provides 2-years of support for early-career African investigators conducting cancer research projects.[22]

Indeed, the radiation oncology workforce in Africa and other LMICs requires consideration. More than 40 countries in both Asia and Africa do not have one trained radiation oncologist, while trained dosimetrists, physicists, and radiation technologists are also limited.[23] Given the high proportion of use of moderate HF reported in our study and the participants' desire for regional training conferences, we propose focused regional sessions on determining eligibility for patients to undergo HF, with a specific focus on the stage of disease and breast size. The exchange of regional knowledge may also improve workforce retention.

Participants also voiced concern about toxicity to the heart, lung, and skin in breast cancer and toxicity to the rectum in prostate cancer. Within the CFIR domain of inner setting and individual characteristics (domains 2 and 5), our study highlighted that personal experiences with toxicity (sometimes caused by the inability to manage motion) were a significant barrier to the use of HF. One proposed solution included developing a consensus guideline on expectations and management of acute and late toxicities from HF for breast cancer, specific to the skin of Africans. For prostate cancer, focusing on mitigating rectal toxicity through the utilization of fiducial markers or training on advanced on-treatment imaging could improve confidence in the use of HF. Another method of combating hesitancy and lack of personal experience was suggested through the role of regional mentorship in the domain of implementation (CFIR domain 4).[24] Trials like HypoAfrica,[25] which look to evaluate the use of HF in prostate cancer in Africa, are enrolling and accruing participants to demonstrate the impact that HF can have in the region. Our study also highlighted the challenge of maintaining and repairing linear accelerators, prompting the need foron-the-ground expertise or quick access to troubleshooting engineers (outer setting, CFIR domain 3).[26]

The results of this data should be interpreted within the context of the limitations of this qualitative study. We acknowledge that the 11 countries represented here are different in their populations, resources, technology, and personnel. We also acknowledge that some countries have only 1 participant and are not representative of all physicians. While these differences exist, the themes highlighted here were prevalent across most interviews in order to provide insight into the highest priority areas. Further qualitative data gathering from physicists, radiation therapists, nursing staff, and patients would be recommended to understand the impact of these prioritization areas to assist in the successful implementation of HF. Finally, we did not discuss the utilization of ultrahypofractionation (for prostate cancer, 5 or 7 fractions, and for breast cancer, 5 fractions) at length. While some centers volunteered that they had started using this on a few patients, this was in the minority, and we could not draw conclusions from this data.

Conclusions

Our results demonstrated that there is currently a high uptake of moderate HF in radiation oncology clinics in SSA for breast cancer and a low uptake of moderate HF for prostate cancer. Participants in clinics with access to IMRT were more likely to use HF for prostate cancer. While the use of advanced technology was important, awareness of HF among referring providers and patients was equally important. For both breast and prostate cancer, emphasis on increased data from Africa, consensus on technique and technology, mentorship models, toxicity counseling, and reimbursements were highlighted as critical considerations.

Disclosures

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Supplementary materials

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