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Abstract

Background: Limited radiation therapy resources have resulted in an interest in developing time and cost-saving innovations to expand access to cancer treatment, in Latin America. Therefore, hypofractionated radiotherapy (HRT) is a possible solution, as this modality delivers radiation over a shorter period of time.

Materials and methods: A selected panel of Latin American (LA) experts in fields related to HRT were provided with a series of relevant questions to address, prior to the multi-day conference. Within this meeting, each narrative was discussed and edited, through numerous rounds of discussion, until agreement was achieved.

Results: The challenges identified in increasing the adoption of HRT in LA include a lack of national and regional clinical practice guidelines and cancer registries; a lack of qualified human resources and personnel education; high up-front costs of equipment; disparate resource distribution and scarce HRT research. An analysis for these overarching challenges was developed and answered with recommendations.

Conclusion: Extending the adoption of HRT in LA can provide a path forward to increase access to radiotherapy and overcome the shortage of equipment. HRT has the potential to improve

population health outcomes and patient centered care, while offering comparable local control, toxicity, palliation, and late effects for multiple indications, when compared to conventional RT. Concerted efforts from all involved stakeholders are needed to overcome the barriers in adopting this strategy in LA countries. The recommendations presented in this article can serve as a plan of action for HRT adoption in other countries in a similar situation.
Key words: hypofractionated radiotherapy; Latin America; access; cancer care; oncology

Introduction

Latin America (LA) is a diverse geographical region with over 600 million inhabitants; characterized by social, economic, and political instability, influencing disease behavior and access to health services. A series of sociodemographic changes, such as an aging population, urbanization, and economic growth has led to a rapid upward shift in LA's cancer burden [1]. Almost 1.5 million new cases and over 700,000 deaths due to cancer occur annually in the region. The five most common malignancies in LA are prostate, breast, colorectal, lung, and stomach [2]. Radiation therapy (RT) plays an important role in the treatment of these cancers whether the approach is curative, influencing local tumor control and overall survival (OS), or in the context of palliative care, where the main objective is symptoms relief and quality of life improvement [3]. The number of cancer cases in the region, and therefore of patients requiring RT, will increase by 67% from 2012 to 2030 [4].

However, access to RT in LA is limited due to a substantial deficit of RT resources in the region. As of 2020, there were only 647 RT centers in LA, proving largely insufficient for the approximately 750,000 new patients that will require RT annually. In some LA countries, up to 5 million people depend on a single RT machine, leaving many without access to treatment [5]. Contrastingly, high income countries, such as the United Kingdom, have 8.1 RT machines per 1 million inhabitants [6]. Geographical disparities in the distribution of these centers further exacerbate this deficit, most noted in rural areas [5]. Hypofractionated radiotherapy (HRT) has been increasingly used for cancer treatment, and as a solution to increase access to the limited RT resources. In this modality, the total radiation dose is distributed into fewer fractions, either using moderate (2.5–3 Gy/fraction) or extreme hypofractionation (> 5 Gy/fraction). Thus, HRT is given over a shorter period of time than conventional RT, increasing convenience for patients, decreasing staffing demands, extending equipment capacity, and increasing access, which is crucial in resource-limited settings [7]. As a result, it may be considered a resource-efficient alternative that conserves the comparable treatment outcomes as standard RT in some specific scenarios. This review will analyze the challenges and opportunities of increasing the adoption of HRT for cancer care in LA.

Methodology

Americas Health Foundation (AHF) along with the Latin American Society of Radiation Oncology (ALATRO) identified a panel of eight experts in radiation therapy with backgrounds in clinical oncology, radiation oncology, public health, and bioethics from Argentina, Brazil, Chile, Colombia, Mexico, and Peru. They were convened for a three-day virtual meeting to discuss if widespread adoption of hypofractionated radiotherapy protocols in oncology could serve as a solution to increase access to radiotherapy in LA. To identify the panel, AHF conducted a literature review using PubMed, MEDLINE, and EMBASE to identify scientists and clinicians from the above countries who have had publications relating to hypofractionated radiotherapy in oncology since 2016. Augmenting this search, AHF contacted opinion leaders in the medical field from LA to corroborate the list of individuals adequately represented the necessary fields of study. All of the experts who attended the meeting are named authors of this paper. An AHF staff member moderated the discussion. The authors retained full control over the content of the paper.

AHF developed specific questions to address the challenges and opportunities related to the adoption of hypofractionated radiotherapy protocols in LA and assigned one to each panel member. A written response to each question was drafted by individual panel members, based on the literature review and personal expertise. Each narrative was reviewed and edited by the entire panel during the three-day conference through numerous rounds of discussion until full agreement was reached. For issues where there was disagreement among the panel, additional discussions took place until all panel members agreed to the content included in this paper. The recommendations developed were based on the evidence gathered, expert opinion, and personal experience and were approved by the entire panel. After the conference, the final manuscript was distributed by email to the panel for review and approval.

Search strategy A

HF conducted a literature review using PubMed, MEDLINE and EMBASE for any publications on molecular testing for solid tumors. The following search terms were used: “radiation oncology”, “hypofractionated radiotherapy” and “hypofractionation”, in combination with “Latin America”, “Mexico”, “Colombia”, “Argentina”, “Brazil”, “Chile”, and “Peru”, from 01/01/2016 until 04/10/2021. Articles identified were in English, Portuguese, and Spanish. Particular attention was paid to identify literature and research in LA.

HRT use and indications

LA’s already-fragile health systems have been severely affected by the COVID-19 pandemic, with lasting effects on budgets and sustainability in the region [8]. Although evidence supporting HRT already existed prior to the pandemic, the contingency instigated a pivotal change to adopt hypofractionated protocols that may continue post-pandemic [9]. In many clinical scenarios, these shorter courses are more patient-friendly, equally efficacious, associated with less financial burden, and similarly morbid to prolonged schedules. Further research to determine how low the number of fractions can go while still being safe and effective is ongoing. Updated information is needed on the regional deficit of new technologies to improve RT overall and propel LA towards new technology implementation.

HRT curative and palliative indications, benefits, toxicity, and limitations are summarized below and in Table 1 for breast, prostate, lung, rectum, central nervous system (CNS), as well as lung, bone, and brain metastases, which are the most prevalent situations where radiotherapy is frequently needed.

Breast

For the last decade, guidelines and randomized trials have supported shorter HRT regimens as the standard for most early-stage breast cancers, as well as locally advanced tumors after neoadjuvant chemotherapy. Randomized trials have confirmed that HRT is equivalent to conventional whole breast irradiation regarding local recurrence, OS, and cosmetic outcomes [10]. Therefore, it has become the new standard of care for most patients instead of conventional fractionation, regardless of laterality, oncologic and reconstructive surgery type, tumor grade, hormone and HER-2 receptor status, margin status, or prior systemic treatment [11–14].

Prostate

HRT for prostate cancer has become of increasing interest due to the potential improvements to the therapeutic ratio [15]. When comparing stereotactic body radiation therapy (SBRT) to conventional fractionation, SBRT shows promising biochemical control and favorable acute and late-treatment related morbidity, at least in low-and-intermediate-risk prostate cancer. The National Comprehensive Cancer Network (NCCN) guidelines were updated in early 2020 to list 5-fraction SBRT as an appropriate regimen for all risk groups of localized prostate cancer, from very low risk to very high risk [16]. In centers without SBRT access, moderate hypofractionation should be preferred over conventional treatment [15, 17].

Lung

Surgical resection is the standard of care for operable early-stage non-small cell lung cancer (NSCLC). SBRT is an option for radical management of inoperable early-stage NSCLC [18]. For locally advanced disease, conventional fractionation with chemotherapy continues to be the standard treatment. There is early data on moderate hypofractionation for locally advanced disease, but more research is still needed in this topic [19]. For palliative treatment, studies suggest that doses of 30 Gy in 10 fractions are associated with modest improvements, when compared to lower doses, mainly in patients with a good performance status. Patients with lower KPS can have a good symptomatic relief with doses varying from 20 Gy in 5 fractions to 17 Gy in 2 fractions [20].

Rectum

In the COVID-19 pandemic, some rectum cancer guidelines have given preference to HRT in most patients who require radiation; others have even gone as far as to recommend 5-fraction RT for all localized rectal cancers, until the pandemic passes [21]. Yet, even in the post-pandemic world, for appropriate patients with resectable upper- to mid-rectal cancers, short-course radiation can become the new standard of care, given its non-inferiority to traditional long-course radiation, with potentially less acute toxicity [22].

CNS

The current standard of care in glioblastoma multiforme management is RT with concurrent and adjuvant temozolomide (TMZ), delivered in 6 weeks [23]. Multiple trials have demonstrated that HRT has a similar efficacy for patients with a low performance status (KPS) or older than 65 years, with treatments lasting from 1 to 3 weeks [24].

Bone metastasis

A large metanalysis, with more than 5000 patients included has shown that a single fraction radiation treatment (SF) yields equivalent pain relief as multifractional regimens (MF). Overall responses have been reported to be 60% in SF and 61% with MF, and complete responses, 23% and 24%, respectively. There were no statistically significant differences in side effects, pathological fracture rates, or spinal cord compression, in either approach [25]. Regarding patients with neuropathic pain, a non-inferiority trial failed to show equivalence between 8 Gy SF and 20 Gy in 5 fractions [26]. Thus, in this group of patients, the 5-fraction regimen can still be an option, as well.

Brain metastasis

The standard treatment for patients with brain metastasis is, if feasible, surgical resection, with postoperative single fraction stereotactic radiosurgery (SRS) of the tumor cavity, although a fractionated treatment may provide superior local control for patients with larger tumor cavities [27]. For non-operated patients, with 1 to 4 brain metastasis (although this limit is debatable), SRS is an interesting option, whole brain radiotherapy (with 5 to 10 fractions) being the standard treatment for the remaining ones [28].

There are other possible indications for HRT, as this is a dynamic scenario, under active investigation, and the list provided here is not exhaustive. But going into further details is beyond the scope of this paper.

RT resource access and availability in LA

Access to radiation facilities in low- and middle-income countries (LMIC) is far from optimal and varies widely between and within nations. In LA, there are vast infrastructural and human resource deficits to meet the RT demands, which underpins the need for access solutions and efficient resource use [29]. Advances such as intensity-modulated radiotherapy (IMRT) and image-guided radiation therapy (IGRT) have improved outcomes and quality of life [30]. However, they come with higher costs and demand more quality assurance, qualified personnel, time per patient, and infrastructure investments. As a result, the treatment capacity of radiation devices decreased [31].

Variations in treatment-center accessibility and patient socioeconomic factors strongly correlate with RT access inequities. RT resource availability is determined by case volume, economic status, healthcare priorities, health expenditure, and national economic welfare, which play a pivotal role in the ability to acquire and maintain RT equipment. A crucial parameter in determining radiation services in each country is the number of people served by each mega-voltage machine (MVM). The International Atomic Energy Agency (IAEA) recommends 1 MVM for every 250,000 people [32]. A ratio of 650,000 inhabitants per MVM was reported in LA. In LA, only Uruguay, a country with a small population, meets the IAEA recommendation [33]. Previous government efforts that have tried to meet the RT demand by acquiring new RT equipment have not been sufficient to overcome the current deficit or the future demand(34), thus emphasizing the need to optimize the existing equipment.

Despite the initial expenses, investing in RT expansion would be cost-effective. Physicians, epidemiologists, and health economists have argued that scaling up RT services over the next 20 years to meet the worldwide demand could save 26.9 million life years in LMICs. Moreover, the economic benefits could total up to 278 billion USD from productivity gains during that same time, thus saving both lives and money [32]. In addition to acquiring new equipment, scaling up can be achieved through optimizing existing equipment use and scheduling.

HRT as a solution to increase RT access

RT access is limited by several factors including geographical center proximity, cost, and availability. Hypofractionation can safely shorten total treatment times and increase the number of patients per device, resulting in high-quality care to a larger number of patients [9].

Recent reviews have focused on cost containment derived from HRT. In addition, HRT presents patients with several benefits including fewer commutes to RT centers. There are potential reductions in out-of-pocket expenses, including commuting costs and income/productivity loss associated with longer treatments. Further savings to care provisions may be associated with a reduced need for patient accommodations, nursing/doctor consultations, and patient-assisted transport schemes [35]. In LMICs, conventional breast cancer costs can be reduced from 2,232 USD to 1,339 USD and prostate from 3,389 USD to 1,699 USD [7]. Cost-calculation models have demonstrated that daily operation expenditures outweigh capital machine costs in RT treatment planning and delivery. Because RT costs are largely a product of time, hypofractionation can reduce the burden of rising healthcare costs. However, the goal of HRT in resource-limited settings is to increase the number of patients treated in a single machine to serve more patients with the available infrastructure [36].

Hypofractionation is most discussed in prostate and breast cancer treatments, which constitute the two largest patient cohorts and a large health system burden [37]. For example, Pakistan has a population of 180 million and 15 medical linear accelerators (LINACs); thus, HRT adoption for breast cancer would result in a significantly higher population OS [38]. Results may be improved if this strategy is extended to other malignancies. Additionally, full hypofractionation implementation in Africa could reduce costs by around 40% and 60% for breast and prostate treatments, respectively. These conclusions can potentially be extended to LA, even though LINAC scarcity is not as pronounced as it is in Pakistan or Africa [7].

This panel concludes, based on this data, that in LA, where access is a pressing issue, technological progress must be accompanied by hypofractionation implementation, considering time, cost-savings, and ethical implications.

HRT basic technology requirements in limited resource settings

The evolution of RT precision has more technical requirements for its provision. Modern treatments require CT-based simulation guidance and LINACs to deliver treatment at a minimum. More advanced technologies, such as IMRT, IGRT, and other upgrades facilitate the introduction of hypofractionation schemes but are not strictly necessary in all cases [39]. Nevertheless, the limited availability of these advanced technologies in LA poses an obstacle to the widespread adoption of HRT, which would most benefit the whole region in terms of efficiency and access [40].

Several technologies are needed to perform HRT safely and effectively. These include CT scan, magnetic resonance imaging (MRI), four-dimension CT (4DCT), cone-beam CT (CBCT), eletronic portal imaging devices (EPID), PET scanners, and immobilization accessories. The consequences of missing a target with HRT are more serious than those of conventional regimens because a greater dosimetric impact may occur, reducing the chances of disease control and increasing treatment toxicity [41]. Table 2 summarizes the basic technology necessary for HRT for different treatment sites. Of note, there is no consensus on the required frequency of target verification, which is a crucial factor to ensure efficacy, safety, and toxicity control. The ideal verification frequency varies based on cancer type and technique used; however, HRT requires at least a weekly verification for moderate hypofractionation; and daily online verification, for extreme hypofractionation or SBRT, based on this panel's experience. Without these minimal requirements, HRT should not be performed due to safety issues.

Reimbursement for HRT

LA health systems are fragmented into subsystems that have different financing, affiliation, and health-care delivery modalities, pervading the region with inequalities [42]. Most public healthcare systems in the region reimburse RT without differentiating the fraction size and technology used. Reimbursement is a major influencing factor for RT prescription, as therapy-cost escalations run parallel with the fractionation schedule [43]. In particular, reimbursement systems that support a fraction-based model or fee-for-service reward more extended treatments [44]. Although LA data is limited, more conclusions can be drawn from international paradigms. For example, in 2011, 57% of patients that underwent breast radiation in the US had unnecessarily costly treatment, accounting for over 420 million USD. HRT protocols in these patients could have potentially reduced these costs by 40% [45]. When examining fraction-based models in Europe, variability was the major and most interesting finding, both in the treatment components considered for reimbursement and in fees that are paid for each treatment technique, fraction, and indication [46]. Although there are no similar studies for LA, the situation is likely comparable.

Thus, reimbursement for RT should be based on bundles or value-based approaches, such as pay-for-performance or outcome-based payments, instead of a fraction-based model [47]. A Brazilian study noted that the change from fee-for-service schemes to bundle payment strategies was reflected in the prescription of shorter schedules, benefitting low-resource settings [48]. However, this shift to bundle reimbursement is not a risk-free operation. Theoretically, it could lead to undertreatment, prioritization of less complex cases, and decrease in quality of care [49]. Therefore, medical audit programs and adherence to CPG are imperative to mitigate these risks [50].

Challenges to the widespread adoption of HRT in LA

Although HRT has demonstrated the potential to improve population health outcomes and access to RT, challenges to its widespread adoption in LA exist. Research on access barriers to

RT are insufficient in LA, and a lack of stakeholder awareness remains regarding HRT's potential to maximize the utilization of existing equipment. In addition to the major reimbursement barrier previously discussed, the principal barriers to the widespread implementation of HRT in LA are:

Lack of national and regional CPG and cancer registries

National and regional CPG on RT are largely lacking in LA, especially for HRT. These are necessary to streamline care and could result in cost and time savings, optimal use of resources, and quality improvement. An informed healthcare community is vital for incorporating new technology. Adherence to guidelines and protocols is imperative to avoid adverse outcomes, especially when adopting complex modalities such as HRT. This shift can only happen if the diverse perspectives of patients, clinicians, healthcare leaders, and payers are integrated to create feasible and sustainable solutions. Furthermore, resources for planning and implementing evidence-based cancer control programs are not available in most LA counties. Only 6% of the LA population is covered by PBCRs, compared with 32% of the European population [51].

Lack of human resources and personnel education

There is a significant shortage of radiation oncologists, medical physicists, radiation therapists, nurses and other staff involved in RT. As RT infrastructure scales up, so will the need for an increased number of specialist and medical training programs in each country. Similar to RT equipment distribution, there are also marked geographical disparities in human resource distribution. Furthermore, knowledge and awareness on HRT in LA is currently deficient but crucial to successfully implement HRT [52]. Current evidence on HRT has not yet translated into clinical practice in part because of an intrinsic resistance to change by the medical community, which may be ameliorated by the inclusion of HRT in local CPG.

High up-front costs of equipment

The high up-front costs to acquire the necessary infrastructure for RT is a major barrier to increasing access. Although HRT provides a solution to optimize the use of existing equipment, increasing the installed capacities of radiotherapy equipment in most countries is still required. The technology acquisition gap is further widened because equipment is negotiated and acquired in USD by weaker currencies and depend on the market size, putting smaller markets at a disadvantage. A 2021 survey reported that radiation oncologists from LMICs were significantly less likely to use hypofractionation than Europeans. Among LA respondents, lack of technology is the most common barrier for hypofractionation use [52].

Disparate resource distribution and access

In LA, there are geographical disparities between the number of machines available in larger cities versus rural areas, resulting in unequal RT access in general and often leaving rural areas underserved [53].

Scarce HRT research

Local research on the HRT outcomes in the LA population is very limited. This is not a barrier exclusive to HRT but directly impacts its implementation. Numerous barriers exist that hinder clinical trial design and execution in the region. Moreover, funding for HRT research is scarce.

Recommendations

HRT protocols provide a path to yield significant cost savings, while offering comparable local control, toxicity, palliation, and late effects for some indications when compared to conventional RT. As we have seen, HRT advances the objectives of patient-centric care, timeliness, efficiency, and equity, providing valuable advantages in patient convenience [7, 9]. The COVID-19 pandemic accelerated changes that catalyzed the implementation of these protocols and prioritized patient-center care and, ideally, should continue in post-pandemic practice. Decision-makers should consider feedback from physicians and medical societies, patients, other governments, academic institutions, and technology suppliers to include different perspectives, which will aid in prioritizing the correct equipment to impact public health needs long-term. The panel proposes the following recommendations to increase the adoption and awareness of HRT in LA. A summary of the challenges, benefits, and recommendations to increasing the widespread adoption of HRT can be found in Figure 1.

1. **Develop national and regional clinical practice guidelines (CPG) that address HRT**

National and regional CPGs must be developed and continuously updated to facilitate HRT implementation. This can be done by adapting international CPGs to local contexts and establishing access landscape through collaboration between national radiation societies, the LA Association of Therapeutic Radiation Oncology (ALATRO), and LA governments. CPGs must consider and provide recommendations on the most cost-effective and resource-efficient protocols. Health institutions must require guideline adherence and implement internal audits to ensure accountability.

2. **Provide continued medical education and training opportunities**

Evidence-based education on HRT for radiation oncologists, physicists, and therapists must be provided to ensure its safe and effective delivery [52]. Effective clinical decision support is needed to address knowledge gaps that contribute to unequal access to RT, specifically targeting practitioners, payers, and decision-makers. Mandatory continued medical education and training must be part of the HRT development plans for RT providers. Additionally, academic programs must be standardized to guarantee that all receive accurate training on implementing HRT protocols.

3. **Update RT reimbursement models**

Reimbursement modalities must prioritize resource optimization and population health outcomes. RT reimbursement should be based on the bundle payments or value-based approaches, such as outcome-based-payments or pay-for-performance instead of fee-for-service models [47].

4. **Infrastructure investments and acquisition**

An increasing cancer burden and the consequential increased demand for RT will render new device purchase necessary, as the current available RT equipment throughout the region is not sufficient and has a limited lifespan [4]. LA countries must collaborate to engage in collective regional negotiations to offset the high cost of RT equipment and mitigate small market disadvantages. Furthermore, updating existing RT equipment makes the radiation process more efficient and requires comparably lower investments.

5. **Address geographical disparities of RT infrastructure and human resources**

The shortage of radiation oncologists, physicists, and therapists can be addressed by creating opportunities in local training programs for RT specialists. Telemedicine could provide a path forward to breach the gaps created by geographical maldistribution of RT resources by implementing remote RT treatments planned and supervised by radiation oncologists and physicists.

6. **Increase local research**

Research on RT schedules with a focus on shortening total fractions for different tumor sites should be a priority in LA to lay the groundwork for evidence-based decision-making. Governments should fund national databases to collect reliable data and statistics to characterize the use of RT, including HRT outcomes. This real-world data will, presumably, benefit physicians, payers, manufacturers, and regulatory agencies.

7. **Consider alternative fractionation protocols and scheduling optimization**

HRT is not a one-size-fits-all solution. Tumors have different α/β ratios and, thus, may respond differently to different radiation schedules, which should be considered while administering RT. While hypofractionation is better suited for tumors with lower α/β ratios, such as those originated in the breast or in the prostate [54], alternative fractionations can be studied for tumors with higher α/β ratios, providing more solutions. The quest for developing time- and cost-saving innovations, such as hyperfractionated or accelerated RT [55], to expand access to limited RT resources must continue.

Besides, radiation is delivered, traditionally, in daily fractions from Mondays to Fridays. This has radiobiological explanations beyond the scope of this paper [56], but, in the era of precision medicine, this uniformity may be more social or political than scientifically planned. If weekends are implemented, adding 2 more days, productivity has the potential to proportionately increase by up to 40%. Patients with oncologic emergencies could take advantage of this new organization and be treated during holidays and weekends, potentially improving palliative results with a small added cost, mainly related to personal, and reducing wait times for other new patients [57].

Conflicts of interest

The co-authors declare no conflicts of interest.

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Table 1. Curative and palliative indications of hypofractionated radiotherapy (HRT)

	Tumor	Indication	Technique	Radiation dose and fractionation	References
Curative treatment					
	Breast	Early	3D or IMRT	Extreme hypofractionation: 26 Gy in 5 fx	[58]
				40–42.5 Gy at 2.5 to 2.6 Gy/fx with an option of a boost	[11]
		Locally advanced	3DCRT or IMRT	40–42.5 Gy at 2.5 to 2.6 Gy/fx with an option of a boost	[11]
		Ductal carcinoma in situ	3DCRT or IMRT	40–42.5 Gy at 2.5 to 2.6 Gy/fx	[59]
		APBI	3DCRT, IORT, brachy	30 Gy in 5 fx QOD, 38.5 Gy in 10 fx BID, IORT: 20 Gy/1 fx	[60]
	Prostate	Low and intermediate risk	SBRT	36.5–40 Gy/ 5 fx	[61]
			3DCRT, IMRT	70.2 Gy/26 fx or 60 Gy/20 fx	[15, 62]
			Brachy	LDR with iridium: 145 Gy; HDR: 38 Gy/4 fx BID	[17]
	Lung	Early, inoperable, central	SBRT	45-60 Gy/5–8 fx	[18]
		Early, inoperable, peripheral	SBRT	45-60 Gy/3–5 fx	[18]
	Rectal	High risk or node-positive	3DCRT or IMRT	25 Gy/5 fx followed by surgery	[21]
	CNS	> 60 years, no systemic therapy	3DCRT or IMRT	40 Gy/15 fx	[24]
		Older/frail	3DCRT or IMRT	25 Gy/5 fx	[24]
Palliative care					
	Thorax	Good KPS	3DCRT, IMRT	30 Gy/10 fx, 40 Gy/15 FX, 50 Gy/20 fx	[20]
		Poor KPS	3DCRT, IMRT	20 Gy/5 fx; 30 Gy/10 fx; 17 Gy/2 fx	[20]
	Bone	Uncomplicated metastasis	3DCRT, SBRT	8 Gy/1 fx	[25]
		Neuropathic pain	3DCRT	2 Gy/5 fx	[26]
	Brain	Resected	Radiosurgery/FSRT	SRS Gy; FSRT of 27 Gy/3 fx or 30 Gy/5 fx (larger cavities);	[27]
		Nor resected	Radiosurgery/FSRT	15–22 Gy/1 fx; 25–30 Gy/3–5 fx	[28]
		Whole brain irradiation	3DCRT or IMRT	30 Gy/10 fx or 20 Gy/5 fx	[28]

CNS — central nervous system; APBI — accelerated partial breast irradiation; 3DCRT — tridimensional conformal radiotherapy; IMRT — intensity-modulated radiation therapy; IORT — intra-operative radiation therapy; brachy — brachytherapy; SBRT — stereotactic body radiation therapy; FSRT — fractionated stereotactic radiation therapy; QOD — every other day; BID — twice-a-day; Gy — Grays (radiation dose); fx — fractions

Table 2. Minimal technological requirements to perform hypofractionated radiotherapy (HRT) in resource limited settings

Treatment site	Contouring	Patient Localization	Treatment technique	Ref
Breast	CT scan	Skin mark	3DCRT	(11)
Prostate	CT scan	2D-EPID*	3DCRT	(63)
Lung/Thorax	CT scan**	CBCT	3DCRT Conformal arc	(64, 65)
Bone	CT scan or CT scan and MRI***	CBCT	3DCRT/ Conformal arc or IMRT (spine)	(66, 67)
CNS	CT scan and MRI	2D-EPID****	3DCRT/ Conformal arc	(68)
Rectal	CT scan	skin mark	3DCRT	(69)

CT — computed tomography; 3DCRT — three-dimensional conformal radiotherapy; CBCT — cone beam CT; MRI — magnetic resonance imaging; EPID — electronic portal imaging device; CNS — central nervous system; * In moderate hypofractionation with online verification.; **with slow CT scan or with the inhale and exhale breath-hold method; ***MRI should be used in spine SBRT and if the target is not well visualized on CT; ****not appropriated for single fraction radiosurgery procedures

Figure 1. Situation map for increasing the adoption of hypofractionated radiotherapy (HRT) in Latin America