Lancet Oncology Commission on Radiotherapy and Theranostics

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Conflicts of Interest

Outside of the submitted work: HH serves (unpaid) on External Advisory Board of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, International Advisory Board of the University of Vienna, Scientific Committee of the DKFZ (German Cancer Research Center), Board of Trustees of the DKFZ, Advisory Board of The Lancet Oncology; reminerated member of Board of Ion Beam Applications; stock options and Board of iCAD; reports research funding to Institution from NIH/NCI.
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Contributors

The IAEA Secretariat convened the Commission. May Abdel-Wahab and Andrew Scott were co-leaders of the Commission and co-developed and co-wrote the study design with input from co-authors. May Abdel-Wahab prepared the initial Commission concept. May Abdel-Wahab, Andrew Scott, Diana Paez, Mauro Carrara, Egor Titovich, Francesco Giammarile collected and/or analyzed data. Nayyereh Ayati, Jing Jing Li, Malina Mueller, Platon Peristeris, Dennis Ostwald, Varsha Hande, Sondos Alkhatib conceived the modelling approach and led the modelling. May Abdel-Wahab, Andrew Scott, Francesco Giammarile, Hedvig Hricak, Mauro Carrara, John Buatti, Ajay Aggarwal, Roberto C. Delgado Bolton, Thomas Eichler, Soehartati Gondhowiardjo, Ola Holmberg, Peter Knoll, Jolanta Kunikowska, Miriam Mikhail, Arthur Rosa, Marcos Santos, Mike M Sathkege, Verna Vanderpuye, Jennifer Yu, Yolande Lievens, Mary Gospodarowicz wrote and/or edited manuscript's sections. All authors contributed and approved the final version of the submitted manuscript.

Search strategy and selection criteria

References were identified through searches of PubMed with the terms “radiotherapy”, “theranostics”, “radiotheranostics”, between Jan 1, 2010 and May 16th, 2024. Articles were also identified through searches of the authors' own files. Only papers published in English were reviewed. Data from PubMed searches was used for background information, and inputs for the modelling in Sections 2 and 3. The final reference list was generated based on originality and relevance to the broad scope of this article.

Executive Summary

The Lancet Oncology Commission on Radiotherapy and Theranostics follows up on the Lancet Oncology Commission on Global Radiotherapy and was created to assess the current status of access and availability of radiotherapy, and theranostics at a global level. A marked disparity in the availability of radiotherapy machines between high-income and low- and middle-income countries (LMICs) was identified. Workforce requirements were also highlighted as a major factor in effective implementation of radiotherapy, particularly in low- and middle-income countries. Broad implementation of hypofractionation techniques compared to conventional radiotherapy in prostate cancer and breast cancer was calculated to result in potentially an additional 2.2 million (0.76 million prostate and 1.40 million breast) patients who could be treated with the same resources, highlighting the importance of implementing new technology in LMICs. A global survey revealed that the current utilisation of radiopharmaceutical therapy, other than ^{131}I, was highly variable in high-income and LMICs, with supply chains, workforce and regulatory issues impacting on access and availability. The capacity for radioisotope production was highlighted as a key issue, and training and credentialling of health professionals involved in theranostics is required to ensure equitable access and availability for patient treatment. We propose actions and investment that would enhance access to radiotherapy and theranostics particularly in LMICs, to realise health and economic benefits and reduce the burden of cancer as a result of accessing these treatments.

Introduction

It is estimated that 50-70% of all cancer patients need radiotherapy (RT) worldwide, from curative treatment to palliation.[1] More than half of this population resides in low- and middle-income countries (LMICs). In low-income countries (LICs), more than nine out of ten cancer patients lack RT access.[1] RT is crucial to achieving the targets of major global cancer initiatives, including those for cervical, breast, colorectal, and childhood cancers. Dialogues on the overarching cancer control global agenda should therefore feature RT among core elements, additionally bearing in mind that a robust diagnostics base, including medical imaging, is requisite to all RT delivery.

The Union for International Cancer Control (UICC) established the Global Task Force on Radiotherapy for Cancer Control (GTFRCC) and it eventually became part of the Lancet Cancer Campaign as The Lancet Oncology Commission on Global Radiotherapy.[1] Published in 2015, the Lancet Oncology Commission on Global Radiotherapy was a landmark study that, using advanced metrics and economic modelling, demonstrated a substantial return-on-investment for spending on healthcare infrastructure, specifically financing for radiation therapy as part of a comprehensive blueprint for cancer control plans in LMICs.[2] It also determined that "radiotherapy can be effectively standardized and delivered irrespective of socioeconomic, political, and cultural context". The report also presented a five-point Call for Action that boldly set forth specific goals, three of which specified 2025 as a target date for achievement. And while it would be accurate to say that progress has been made since 2015, much remains to be done.

The use of targeted radionuclides and radiopharmaceuticals delivered systemically or loco-regionally to treat cancer through a theranostic approach has also emerged as a transformative change in the landscape of precision medicine.[3,4] Theranostics combines diagnostic nuclear medicine imaging to validate target expression and estimate radiation dose, and therapeutic approaches to identify suitable patients for treatment, and precise targeting of tumour foci for therapeutic response. The development of radionuclide theranostic agents has seen significant progress, with an increasing number of regulatory approvals and opportunities for new indications. However, there remain considerable challenges in the access and availability of theranostic treatments, particularly in LMICs.[3-5]

Concurrent to these ongoing efforts to upscale RT and introduce theranostic treatments for cancer patients, evidence for upscaling medical imaging including nuclear medicine and its impact on cancer care, was recently reported in the Lancet Oncology Commission on Medical Imaging and Nuclear

Medicine.[6] This Commission found that the comprehensive combined scale-up of imaging, treatments (primarily medicines, RT, and surgery), and care quality would prevent 9.6 million deaths worldwide between 2020 and 2030.[7] It was also determined that scale-up of imaging access would provide a return on investment of $206.1 per $1 invested using a global lifetime productivity gain approach.[8]

In early 2022, the International Atomic Energy Agency's Division of Human Health set out to update the 2015 Lancet Oncology Commission report and assess the progress in achieving the goals it set forth. This update aimed to include discussion on the use of resource sparing hypofractionation (typically doses greater than two Gy per fraction) and of advanced technology such as stereotactic body radiotherapy (SBRT). SBRT is a type of hypofractionation, that delivers precise high doses of radiation in a small number of fractions while minimising damage to a healthy tissue and requires more advanced equipment than conventional hypofractionation. In addition, due to the rapid advances in radiopharmaceutical therapies as a major new approach beyond traditional radiation therapy for treating cancer patients, and the disparate availability of theranostics in many countries, an evaluation of the current status and issues regarding access and availability of theranostics at a global level is clearly required. Consequently, the Lancet Oncology Commission on Radiotherapy and Theranostics was created. Radiotherapy and theranostics have overlap in terms of knowledge of radiation principles and medical physics, and both require a fundamental understanding of radiation biology and how this can be utilised for effective treatment approaches for cancer patients. This Commission comprised a diverse range of experts and representatives from regional radiation oncology and nuclear medicine specialty societies from around the world. Their task was to review the global status of access and availability of radiotherapy and theranostics, and identify strategies to ensure appropriate access for optimal patient care and health outcomes.

Section 1: Barriers to access for radiotherapy and theranostics

Radiation Therapy Techniques and Requirements for Application

Radiation therapy (RT) is delivered by machines external to a patient, teletherapy, as well as internally via implanted seeds (brachytherapy). Teletherapy is the most common form of RT and is delivered by linear accelerators that generate x-rays or more commonly by ^{60}Co gamma irradiation.[9] Techniques for radiotherapy delivery have rapidly evolved over the last 30 years. Modern radiotherapy treatment begins with 3-dimensional imaging data acquired for simulation, consisting of computed tomography (CT), CT alone $\pm$ magnetic resonance (MR) imaging, single photon-emission computed tomography (SPECT) and positron emission tomography (PET/CT). This imaging data is used to identify the tumour and normal organs at risk and subsequently to generate a treatment plan to irradiate the cancer while

sparing normal tissue to minimize complications. This simulation template generated for each patient enables the development of more complex 3D plans delivered from multiple angles or arcs and often modulated in the plane of the beam's delivery to produce intensity modulated treatment (IMRT). The evolution from 2D to 3D to IMRT improves normal tissue sparing and increases curability through dose escalation, but requires complex computer-controlled treatment machines, and corresponding advances in quality assurance and quality control. 2D treatments are planned using a limited number of beams with the boundaries delineated on orthogonal x-rays of the patient.
3-D conformal radiotherapy (3-D CRT) is design and delivery of radiotherapy treatment plans based on 3-D image data such as CT data with shaping of treatment fields to conform to the target tissue. More recently, 3D imaging (including MR, CT and PET) has been integrated into the treatment delivery machines to verify daily targeting of the radiation delivery (image-guided radiation therapy – IGRT).[10] The integration of imaging capability has increased the cost and infrastructure (e.g. power, air handling) needed to support these advanced machines.

The ability to link daily treatment images to treatments has improved RT delivery accuracy and precision. As a result, hypofractionated regimens (<5 fractions) are now being applied throughout the body. This is referred to as stereotactic body radiotherapy (SBRT). Fewer fractions enables more patients to be treated on a single machine and can therefore improve patient access. Real-time imaging of respiration and peristalsis (4D) has also been integrated to further enhance RT delivery accuracy and precision. These technological advances can reduce the volume of tissue irradiated and thereby serve to reduce side effects, particularly when pursuing higher dose per fraction with SBRT. many traditional side effects associated with larger treatment volumes incorporating unintended normal tissue. While the cost of technical requirements and devices has increased – the capacity to treat more patients effectively with less side effects makes radiotherapy an even more attractive cancer treatment for LMIC. Enablers of safe adoption of these new high performance techniques in resource constrained regions include enforcement of stringent quality assurance protocols, proficient and adequate workforce, and maintenance of equipment. Enabling high quality radiotherapy entails avoiding buying radiotherapy machines with no service contract, as it is a challenge commonly encountered when buying second hand machines. In addition, retention initiatives to retain skilled staff are essential.

Within the last decade, brachytherapy delivery has also integrated high-resolution CT and MR imaging into treatment paradigms and thereby improves dose distribution and reduced toxicities. This is a significant advantage for cervical cancer, which is highly prevalent in LMICs and where brachytherapy is a vital component of management. Particle beam therapy can also spare normal tissues and have wide therapeutic benefits for cancers.(PMID: 37269856) Unfortunately, the initial cost and continued requirements for maintenance and enhanced expertise are impractical for LMICs who struggle to maintain and acquire even conventional radiotherapy equipment.

Radiotherapy requires competent professional staff to ensure safe and effective patient treatment and management. The safe and effective use of radiotherapy treatment requires quality assurance in the context of radiation-related technologies, radiation therapy dose planning and verification, diagnostic image optimization and dose reduction, and data management and analysis.[11] The global shortage of Medical Physicists is considered one of the major barriers to increasing access to RT disproportionally impacting LMICs. This is in addition to additional barriers to RT access including equipment, infrastructure and other workforce availability.

Survey of Radiotherapy Equipment

The International Atomic Energy Agency (IAEA) has established a Directory of Radiotherapy Centres (DIRAC), which provides information on the current status of radiotherapy centres and equipment globally.[12] The DIRAC database shows there are approximately 8,800 radiotherapy centers, over 16,280 teletherapy, and about 3,470 brachytherapy resources globally (Figure 1). These numbers paint a stark picture of disparity: whereas in high-income countries, one teletherapy machine serves around 130,600 people, in low-income countries, this ratio plummets to one machine for every 15.6 million individuals. The abundance of medical Linear Accelerators (LINACs) in well-resourced landscapes correlates with advanced healthcare systems that have the capital to invest in comprehensive cancer care. The high ratio in these regions not only indicates the quantity of available equipment, but also the potential for timely and quality cancer treatment, which are critical factors in improving patient outcomes. This imbalance underscores the need for expanding radiotherapy facilities in low and middle-income countries, where access to radiation oncology is markedly limited, thereby hindering delivery of adequate cancer care for the population.

The global disparity in the availability of radiotherapy machines is further complicated by the distribution within countries, which is often concentrated in large urban centres, leaving smaller rural and remote populations underserved. Additionally, the presence of radiotherapy machines does not strictly ensure availability, with hurdles such as access to servicing and maintenance, running costs, and healthcare staffing limiting access. This global disparity in radiotherapy access underscores the urgency for an international collaborative effort to meet the minimum standards set for cancer care. Resource-rich countries and global health organizations should prioritize the mobilization of resources, technology transfer, and expertise dissemination to bolster radiotherapy services where they are most needed. By acknowledging these disparities and committing to action, the global health community can make significant strides toward equitable cancer care for all.

Radiotherapy adoption

Distribution of high energy external beam radiotherapy machines across country income groups is shown in Figure 2. In general, data show that over the last decade there has been a trend towards the target of 1 machine every 500 cases needing radiotherapy for any one of the income groups. The number of ^{60}Co machines dropped among all income groups, with LMICs showing however an improvement in number of LINACs and overall access to radiotherapy. Nevertheless, there is a clear gap, which is higher for less resourced countries. On average, low-income countries would need more than 8 times the number of currently available radiotherapy machines to be able to reach the target of 1 machine every 500 cases needing radiotherapy. Of note, the trend is that high-income countries are approaching the value of 1 machine every 500 cases needing radiotherapy by reducing their machines. This may reflect optimisation and centralization of radiotherapy resources.

The distribution of radiotherapy machines in United Nations (UN) regions is shown in Figure 3. The trends are quite heterogeneous across different regions. The overall trend in reduction of ^{60}Co teletherapy machines is however confirmed, though Central and Southern Asia is the region with the highest proportion of ^{60}Co equipment still operational in 2023. Sub-Saharan Africa is the region showing the highest gap with 20 countries having no radiotherapy equipment, whereas Northern America is the region with the highest proportion of radiotherapy machines per patient, even with a drop in number from 2013 to 2023. Figure 1 shows the availability of radiotherapy machines per million people across the globe revealing a tapestry of inequity in cancer care resources. Figures 2 and 3 highlight the gap in radiotherapy equipment as discrepancy between the availability of radiotherapy services and the actual patient's needs. In addition to addressing the gaps in equipment, appropriate maintenance is essential to minimise machine downtime (Panel 1).

Linac age, availability of imaging and motion management capabilities

The availability of imaging and motion management capabilities are important elements for delivery of precision radiotherapy and data are needed to assess the situation globally but are not widely available. Thus, as part of postal dosimetry audit programme, starting in 2022 all participants who had a linear accelerator audited by the IAEA dosimetry laboratory in the biennium 2021-22 were surveyed. The goal was to collect available information on the technological capabilities of linear accelerators globally, with a particular focus on LMICs and to complement DIRAC data. Data was collected on imaging and motion management capabilities of linear accelerators. There were 707 audit participants surveyed across 77 IAEA Member States, and 512 responses were received from 70 countries. The distribution of the replying participants in terms of country income level was high income (HI) 163, upper-middle income (UM) 197, lower-middle income (LM) 149, and lower income 3. The geographical distribution of replying participants was Europe and Northern America 193, Southeast Asia, East Asia and Oceania 119, Northern Africa and Western Asia 78, Latin America and Caribbean 59, Central and Southern Asia 46, and Sub-Saharan Africa 16.

Age of equipment

The survey shows a higher average equipment age in more resourced countries (Figure 6). If machines are well-maintained, the expected lifecycle is 10-15 years.[18] The lower average equipment age for LMICs might reflect either new installations or recent updates to existing infrastructure. It may also reflect the design of the survey and characteristics of respondents. Central and Southern Asia as well as Sub-Saharan Africa show the lowest equipment age, whereas Latin America shows the highest one, exceeding 8 years.

Image Guided Radiotherapy (IGRT) capabilities

The availability of imaging and motion management capabilities is required for delivery of precision radiotherapy The survey revealed that most of the machines, regardless of the region and income level they belong to, have IGRT capabilities (Figure 6c and 6d). IGRT equipment varies in complexity, ranging from basic systems that can only generate MV planar images, which have lower contrast compared to kV systems (such as MV portal imaging, limited primarily to visualizing bony structures), to more advanced systems with volumetric imaging capabilities (kV and MV cone beam CT).[18] IGRT allows setup of the patient and recreates as much as possible the conditions established for treatment during the planning phase. The more complex the technology, the higher the accuracy in positioning the patient for radiotherapy treatments and the more demanding is the staff training as well as the economic resources needed.[19] Of note, some treatment modalities, including IMRT and VMAT, require IGRT as a prerequisite for safe and accurate treatment delivery.[18] The survey does not differentiate between different IGRT technologies (e.g. MV portal imaging, planar kV, kV and MV cone beam CT), however, it clearly shows wide availability of IGRT capabilities.

Motion management capabilities

When radiotherapy is used to treat targets that might move (e.g. prostate) or are moving (e.g. lung, breast) in the timeframe of treatment delivery, accuracy achieved with pre-treatment imaging may even be improved by the use of motion management techniques.[20] These techniques allow tracking the target position during treatment and adapting the delivery in real time or interrupting it if the target exits a pre-determined spatial interval. Access to any kind of motion management capability across the UN regions and country income groups is presented in Figure 6e and 6f. It is important to note that this technology involves higher equipment and staff training investments than IGRT alone and as shown in Figure 6f, there is a clear trend towards greater availability with HIC adopting this technology more frequently.

Workforce Requirements

Evaluating radiotherapy requirements and needs at a national and wider levels is the initial phase in effectively planning processes, workforce, and infrastructure. Utilizing data-driven planning for health care offers significant possibilities, yet also presents numerous complications in the collection and assessment of data.[21,22] Significant discrepancies in the availability of megavoltage machines as well as numbers of health professionals including radiation oncologists and medical physicists per million population can be seen.[23,24] Furthermore, it is difficult to collate data on human resources across countries given the complexity of the process and different tasks assigned to different health professionals in the radiation oncology workforce.[25] This issue of available workforce contributes to the statistic that approximately one in four cancer patients lacks access to evidence-based radiotherapy.[26] Hence, it is important to modify treatment techniques to increase access and minimise workload in order to extend staff capabilities.

Data from UN agencies, including cancer incidences reported in Global Cancer Observatory (GLOBOCAN) by the International Agency for Research on Cancer (IARC), gross national income and income levels from the World Bank, and operational status of megavoltage teletherapy machines through the IAEA DIRAC was used for a global radiotherapy workforce demand analysis.[11,27,28] Previously established methodologies established in reported in the literature were utilised to construct the model and perform calculations in both aggregated and country-level for a comprehensive understanding of the global landscape of radiotherapy workforce needs.[29-32] In 2022, the radiotherapy workforce was estimated to consist of 51,091 radiation oncologists, 28,384 medical physicists, and 85,151 radiotherapy technologists. Looking ahead to 2050, the global projection indicates a substantial increase in new cancer cases, results reflect a more than 60% surge of radiotherapy workforce demand, including 82,287 radiation oncologists, 45,715 medical physicists, and 137,145 radiotherapy technologists globally. On a regional scale, the greatest demand for radiotherapy professionals in 2050 is expected in Eastern Asia (28.0% of the global workforce) due to the large population size and the resultant projected increase in cancer incidence, followed by South-Central Asia (15.1% of the global workforce), North America (12.0% of the global workforce), South America (6.4% of the global workforce), South-Eastern Asia (6.1% of the global workforce), Western

Europe (5.4% of the global workforce) and Sub Saharan Africa (4% of the global workforce). The largest proportion of the radiotherapy workforce in 2050 is predicted to be in upper-middle-income countries (101,912, 38.8%). Additionally, 88,915 (33.9%) radiotherapy professionals are anticipated in high-income countries, 61,452 (23.4%) in lower-middle-income countries, and 10,345 (3.9%) in low-income countries. Urgent strategies are imperative to empower the global healthcare workforce, guaranteeing the safe treatment of present and forthcoming patients, and upholding the fundamental human right to access suitable healthcare. The importance of this was recently emphasised by the survey report of the International Organization for Medical Physics (IOMP), where 73.4% of responding medical physics organizations worldwide reported a shortage of medical physicists. In addition, innovation in training and solutions to the lack of recognition or certification can positively affect the availability of personnel. Of course, innovations whether in training and human resource uses, automation of processes including contouring and planning, as well as the expanding use of AI, can all further expand the available human capacity.

Population needs

The demand for radiotherapy services is determined by cancer epidemiology, population age, availability of diagnostic services, access needs, and the country's socio-economic development. The radiotherapy utilisation rate (RUR) varies among countries, but in general, 50% of new cancer cases will need a first course of radiation, and 15% are re-treated.[33,34] The literature reports shortfalls of RT access even in high-income countries (Canada, Australia, Europe).[24,32,34,35] High-income countries comprise < 20% of the global population yet house 66% of radiotherapy equipment. One radiotherapy machine serves 1 and 5 million patients respectively in LMICs, which aligned with non-compliance with recommended treatment due to the high cost of travel for radiotherapy services in LMICs highlights the need for geospatial equity in equipment, and also adoption of hub and spoke models in service delivery.

Moreover, radiotherapy is often perceived as an expensive treatment modality, whereas this is not supported by evidence from economic analysis. In Europe, radiotherapy consumes 7.8% of the cancer care budget, and less than 0.5% of the total health-care budget (Lievens, Lancet Oncol 2020; 21: e42–54). By 2035, a projected economic benefit of $365.4 billion and $104.2 billion in human capital returns if radiotherapy services were scaled up in LMIC.[2] The lack of inclusion of radiotherapy services as a vital component of national cancer control plans is a significant deficit in effective uptake and maintenance of radiotherapy services. As a policy document, recommendations are indeed more likely to be implemented when supported by cancer control plans. In this context, the need for equitable access to new radiotherapy delivery systems capable of safely administering hypofractionated schemes and SBRT to enhance patient access cannot be underestimated. Panel 2 demonstrates the cost-effectiveness of stereotactic body radiotherapy versus conventional radiotherapy for medically inoperable stage I non-small cell lung cancer in Mongolia: a low-middle income country perspective.

Radiotherapy, as an essential part of cancer management, requires significant Investment in terms of the cost of treatment machines and additional resources for developing and maintaining a radiation treatment programme in a sustainable manner. In addition to radiotherapy equipment, this includes management support, trained professionals, and well-maintained facility infrastructure, including an up-to-date quality management system. For planning and provision of radiotherapy service that corresponds to the identified needs, it is crucial that adequate regulatory, selection and procurement systems are in place and followed, both for the new and donated equipment.[42] The optimal utilization rate is important for planning radiotherapy services at the country level. However, once the centres are available, education of the population and awareness of the importance of radiotherapy as part of the cancer management paradigm is essential to ensure the population benefits from access and that cancer patients comply with the treatments.

Theranostics – access and availability

Theranostics involves the simultaneous application of targeted agents for both therapeutic and diagnostic purposes.[43] The adoption of the theranostic concept underscores the necessity for a patient-centric approach to optimize treatment effectiveness and reduce adverse effects in the era of cancer and chronic disease upsurge.[3,4] In the last 10 years there have been major advances in the development of molecular imaging probes suitable for imaging cancer targets, as well as exploring the biology of cancers, and patient suitability for treatment.[43] The development and approval of new radiopharmaceutical therapies for bone metastases, liver cancer, advanced neuroendocrine cancer, and metastatic castrate-resistant prostate cancer have also led to increasing demand for theranostic treatments.[3,4,44] Theranostics has been identified as one of the fasted growing areas of development of potential new cancer treatments, with an increasing number of therapeutics being eveluated in clinical trials.[3,4] Despite these advances, information regarding the access and availability of theranostic capabilities in countries around the world is limited. The production of radioisotopes for imaging and therapy is concentrated in a limited number of countries, creating supply chain challenges. These issues were exacerbated during the COVID-19 pandemic, which restricted access to essential radionuclides in high-income, middle-income, and low-income countries, highlighting the fragility of global supply chains.[5,45-47]

To explore the current availability of theranostics and to establish the current availability, and issues relating to access, training and workforce, the IAEA distributed a questionnaire to nuclear medicine societies in all countries with known nuclear medicine facilities (Supplementary data). Responses were received from 90 countries (28 high-income, 22 upper middle-income, 31 low middle-income and 7 low-income) (Supplementary data). The use of theranostics treatments varies significantly from country to country, and information on the current numbers of patients treated was not easily obtained in some countries. There were, however, clear trends in the use of theranostics across countries (Figures 5-8), and marked differences in use between high-income, middle-income and low-income countries (Table 1.1 and 1.2). The reasons for the lack of availability of theranostic treatments are primarily related to access to radiopharmaceuticals, a lack of a trained workforce, the infrastructure available for treatments, and funding for treating patients with theranostics. While the availability and use of ^{131}I for the treatment of hyperthyroidism and thyroid cancer is evident in most countries (Figure 7), this is in marked contrast to the access to other theranostic treatments in many countries, particularly in Latin America, Africa and Asia (Figure 8-10).

Workforce and training in theranostics

The requirements for the delivery of theranostics include adequate infrastructure and workforce experienced in both the imaging and treatment of patients with radiopharmaceuticals, ideally within a multi-disciplinary team.[48-50] As part of this Commission, we conducted a detailed exploration of the current workforce in nuclear medicine sites across 90 countries.[51] This revealed similar marked differences in numbers of nuclear medicine physicians, medical physicists, nuclear medicine technologists, radiochemists, radiopharmacists, and nurses who are essential for the provision of a theranostics service. A particular need for radiochemists and radiopharmacists was noted, even in high income countries, and medical physicists were also uncommon in middle- and high-income countries. The need for increased workforce for delivery of theranostics to patients has been recognised and some training programs are underway. The appropriate training of medical professionals involved in theranostics delivery to patients requires the development of training programs and criteria for credentialing.[48,50-52] It is necessary for trainees to acquire the necessary skills and knowledge, as well as for established practitioners to maintain a standard level of competency in radiopharmaceutical use, cancer biology, molecular imaging interpretation, dosimetry, and cancer patient management.[49,53] There have been initiatives to establish credentialing in theranostics, and a recent position paper on minimum training standards for clinicians practicing theranostics has been published through an IAEA expert panel process.[52]

Regulatory issues for theranostics

The use of radiopharmaceuticals for imaging and therapy is subject to regulations regarding the production process and quality control testing of the radiopharmaceutical, to ensure the safety and quality of the administered activity, and to ensure the safety of the patient, staff and public.[54,55] Guidelines have been established by the IAEA and WHO for radiopharmaceutical use, and a recent position paper addresses the regulatory requirements for both imaging and therapeutic use of radiopharmaceuticals to ensure both safety and equity of access.[56] These are important issues to address to facilitate the more widespread use of theranostics in numerous countries where radiopharmaceutical therapy beyond ^{131}I therapy is not well established. The need for a suitably trained workforce to ensure production of radiopharmaceuticals is performed to appropriate standards, and the administration of theranostics treatments is performed in a safe and effective manner, is also a requirement of ensuring regulatory requirements are met for hospitals and for the public. [51,54,55]

Section 2: Optimising radiotherapy resources: comparison of hypofractionation to conventional radiotherapy

It has been established in multiple clinical trials that conventionally fractionated (CRT) and hypofractionated radiotherapy (HRT) have equivalent tumour control and similar toxicity profiles across a range of cancers, including breast and prostate cancer.[57-61] HRT is associated with many benefits including lower costs, improved patient access, increased treatment precision, reduced treatment time and reduced costs associated with daily treatment, leading to its inclusion in many guidelines. [60-62] Shorter treatment courses also liberate machine time, thereby improving access to radiotherapy which is particularly important for low and lower-middle-income countries where current access to radiotherapy is limited. In high income countries, the expansion of capacity may fall short of the growing needs due to increasing cancer incidence.[63] The use of 5 fraction regimens in breast cancer may further lead to release of more treatment slots, increasing access. However, the increasing use of SBRT in oligometastatic disease may lead to greater complexity in simulation, planning and set up but can need less fractions as compared to some palliative cases where a longer fractionation; albeit a single fraction given with conventional techniques would be less labour-intensive but with a greater need for retreatment. We therefore undertook a cost-minimisation analysis linked to the adoption of HRT compared to CRT in breast and prostate cancer, to establish the patient throughput advantages and potential global cost benefits associated with this treatment approach, driven by a lower number of fractions per patient.

Estimating the impact of hypofractionation on radiotherapy needs

The annual prostate and breast cancer incidences for each country was determined using data reported in the 2022 GLOBOCAN database, an online resource developed by the International Association of Cancer Registries.[27] Subsequently, the incidence data were adjusted to reflect the 2024 figures, accounting for population growth within each country up to 2024. Optimal radiotherapy utilisation, as outlined in the Lancet Oncology report on access to radiotherapy, served as the basis for calculating the optimal annual number of radiotherapy courses in each country. Notably, for prostate cancer and breast cancer, this rate was determined to be 58% and 87%, respectively.[2] These estimates were considered robust across income groups and potentially conservative for low-income countries despite variations in cancer stage at diagnosis.

The number of fractions per radiotherapy course was determined for both CRT and HRT, drawing upon published guidelines and available literature.[60-63] This was further validated by real-world data obtained from a survey conducted across over 200 radiotherapy centres spanning 55 countries (Supplementary data). For the external-beam radiotherapy of localised prostate cancer, HRT utilising 60 Gy in 20 fractions and CRT employing 74 Gy in 37 fractions (as the established standard of care) were used. In the context of breast cancer treatment, HRT for the whole breast was assumed to use 40 Gy in 15 fractions. This regimen was considered equivalent to employing 25 fractions of 1.8 to 2.0 Gy each in CRT for whole breast / chest wall component of the treatment.[61] Breast boost after breast/chest wall radiotherapy was not added to the radiotherapy analysis in order to avoid the complexity brought upon by the fact some patients would not receive a boost and that those who did have a wide variety of boosting techniques (eg brachytherapy, simultaneous integrated boost, intraoperative techniques). While emerging evidence also support use of ultra-hypofractionated regimens in breast and prostate cancer, we focused on moderately hypofractionated approaches given these are more likely to be able to be adopted without overwhelming additional infrastructure. The selected regimens were also the most frequent CRT and HRT regimens reported in the real-world global survey. Differences in number of fractionations required in each intervention were then calculated and converted into the number of additional patients that could be treated when fully implemented. This consideration of demand does not consider supply side constraints or changes in simulation activities.

Estimating cost savings associated with lower number of fractions with HRT versus CRT

The cost per fraction was determined by referencing the Lancet Oncology paper on radiotherapy access, which utilised an activity-based costing calculator developed by the IAEA.[2,64] This model reported the operational costs in 2015 dollars associated with delivering treatments per radiation fraction in countries categorised as low-income (LI), upper middle-income (UMI), lower middle-income (LMI), and high-income (HI) as per income level definition. We conservatively assumed these proportional costs for radiotherapy remained constant to 2024. This approach aligns with the assumption made by Atun et al., that these costs would apply over a 20-year timeframe (2015-35).[2] Operational costs encompassed expenses related to treatment-delivery operations (operational staffing, including radiotherapy oncologists, medical physicists, radiation therapists, nurses and engineers), equipment (including maintenance and a 12-year amortisation period), and building (including structural maintenance and a 30-year amortisation period). Additionally, a factor of 1.2 was applied to accommodate overhead costs. The operation costs per fraction were estimated to be 60, 65, 86 and 235 US dollars, in LI, LMI, UMI and HI countries, respectively.[2]

No upfront fixed costs were included in our analysis. This decision was primarily driven by the assumption that similar unconstrained resources were being transferred between CRT and HRT. Additionally, it acknowledges that certain capital resources with fixed costs, necessary for delivering radiotherapy, cannot be freed up when fractions are omitted.[65] It was assumed that the freed-up resource capacity resulting from the replacement of radiotherapy approaches would be utilised for treating additional patients.

Cost-savings were quantified as a sum in US Dollars and as a proportion of building, salary, and equipment costs across different income levels. This approach was taken due to the varying shares of these cost components in different income levels. Specifically, salaries account for 65% of costs in HI countries, while in UMI, LMI, and LI countries, they represent 40%, 20%, and 10% of costs, respectively. Equipment costs constitute 30%, 55%, 75%, and 80% of costs in HI, UMI, LMI, and LI countries, respectively. Building costs make up 5% of costs in HI, UMI, and LMI countries, and 10% of costs in LI countries.[2]

Results

The demographics of the countries included in the global burden and need estimations, categorised by income level, are shown in Table 2. The final analysis encompassed 174 countries. These countries were distributed across different income levels: 15% belonged to LI, 27% to LMI, 26% to UMI, and 32% to HI categories. Annual incident early-stage prostate and breast cancer patients and the number of radiotherapy courses required for their treatments are presented in Table 3. Additionally, Table 3 demonstrates the number of fractions required to complete one course of therapy per patient, using CRT and HRT interventions and the difference in number of required fractions and also additional patients that could be treated, if HRT substitutes CRT. It is estimated that a total of 3 million cancer patients (0.9 million prostate cancer patients and 2.1 million breast cancer patients) would potentially require radiotherapy in the year 2024 across all income groups and a considerable variation in needs as demonstrated in Figure 11. Notably, the proportion of the global needs are considerably higher in high-income countries (57% in prostate and 41% in breast cancer, Table 3), possibly attributed to a greater participation of HI countries in GLOBOCAN incidence reporting (32% of the GLOBOCAN's incidence report sample) and also higher diagnosis rates in these countries. Lack of screening, diagnostic and cancer registration programs in LMICs may also contribute to the discrepancy of incident cancers across income groups.

If these patients were to be treated with CRT, it would require 33.1 million fractions for prostate cancer and 52.5 million fractions for breast cancer. In comparison, only 17.9 million fractions for prostate cancer and 31.1 million fractions for breast cancer would be required if HRT is adopted. This represents a notable total difference of 36.2 million fractions required between the two treatment modalities in the two treatment areas. This could also equivalently translate to an additional 2.2 million (0.76 million prostate and 1.40 million breast) patients who could be treated with the same resources employing a hypofractionation treatment strategy. It should be emphasised that these estimations were solely based on considerations of optimal resource availability covering the needs, and it was assumed that the resources required for both interventions were similar and not constrained, and that freed-up resources resulting from the replacement of radiotherapy approaches would be utilised for treating additional patients. Whilst this example illustrates the theoretical potential of adopting HRT in prostate and breast cancer, this should be seen in the context of a more diverse cancer population, where the actual resource availability remains insufficient to cover the actual needs (see Figures 2 and 3). Scarce resources that would be freed by adopting HRT in those cancer types for which there is ample evidence, especially prostate and breast cancer, could then not only be used to make radiotherapy more accessible to prostate and breast patients, but equally so to patients with other cancer types that nowadays lack access to radiotherapy.

Table 4 presents the potential cost-savings resulting from the utilisation of HRT over CRT, focusing on operating costs only. We estimated both total savings and the components, including salary, building, and equipment costs, across different income groups (Figure 12A). Additionally, proportional cost savings are illustrated, considering the gross domestic product (GDP) per capita and per billion population (2024), to provide a more tangible understanding of the results (Figures 12B and 12C). This highlights that while the cost savings are notably higher in high-income countries across both cancers, possibly attributed to a larger number of incident cancer patients and higher costs per fraction which was mainly attributed to higher salaries, they have a significant impact in low-income countries, where the GDP per capita is substantially lower. Furthermore, when the analysis was adjusted for population size in the GLOBOCAN cohort (0.75, 3.51, 2.56, and 1.29 billion people in LI, LMI, UMI, and HI countries, respectively), the impact in LI countries becomes much more significant, particularly in breast cancer. The sensitivity analysis revealed that an 80% and 50% substitution of CRT with HRT could result in potential cost-savings of $2.04 and $1.28 billion for prostate cancer, and $2.37 and $2.48 billion for breast cancer, respectively.

These findings demonstrate a linear association between cost-savings and proportional substitution. The annual incidence of prostate and breast cancer across 174 countries (including 32% HI, 26% LMI, 27% LMIC, and 15% LI countries) was estimated to be 1.5 million and 2.4 million cases, respectively, in 2024. This translates to an estimated annual potential demand of 0.9 million and 2.1 million radiotherapy courses. Substituting CRT completely with HRT could lead to freeing up resources that could theoretically allow treatment of an additional 0.76 million prostate and 1.4 million breast cancer patients. This is driven by a reduction in total number of fractions, assuming the resources required for both interventions were similar and not constrained and the freed-up resources were used to treat additional patients. In the scenario that HRT completely replaces CRT, and potential global demands for radiotherapy are met, this might translate to a total operational cost-saving of $2.55 billion and $2.96 billion for prostate and breast cancer, respectively. Notably, 80% of the estimated prostate cancer-related savings and 68% of breast cancer-related savings are attributed to HI countries mainly due to earlier detection and higher reported cancer incidence in the GLOBOCAN data. However, when considering GDP per capita and population counts, the impact of cost savings, particularly in relation to equipment, became more significant in lower-income countries. It should be noted that incorporating indirect cost savings linked to lost productivity due to travel to radiotherapy facilities would have significantly increased the overall cost savings. However, this was not included given high variability in travel modality and costs across countries impacting applicability. Our results are therefore considered conservative of the potential savings.

Our global study evaluating the cost-savings associated with HRT approach replacement align with those of other studies, which have demonstrated significant cost savings associated with HRT compared to CRT.[66-69] These results also highlight the considerable cost-saving advantages of hypofractionation radiotherapy compared to conventional methods, particularly in low- and middle-income countries. This is especially significant given the unmet need for radiotherapy, particularly in addressing the prevalent cases of prostate and breast cancers. With limitations in infrastructure, equipment, and personnel resources, enhancing efficiency becomes imperative to accommodate a larger patient population within existing constraints. Consequently, the results of this study could inform policymakers in the adoption and integration of HRT in clinical practice. Furthermore, it may prompt the development of more efficient funding of radiotherapy services, such as reimbursement per course of therapy rather than on a per fraction basis to encourage more efficient use of resources per given outcome.

Optimising Resources by extending operational hours

To further optimize radiotherapy resources, it is critical to consider extending the operational hours and adding additional shifts to maximize the use of existing radiotherapy machines. This strategy is particularly feasible in low and middle-income countries (LMICs) where labor costs are significantly lower relative to the high costs associated with radiotherapy equipment. Implementing longer working hours and multiple shifts can greatly increase patient throughput without the need for substantial capital investment in new equipment, thus addressing the urgent need for expanded access to radiotherapy in these regions.

This approach requires careful planning to ensure that the workforce is adequately trained, remunerated and supported, but it presents a cost-effective solution to leverage existing resources more efficiently. By aligning operational practices with the economic realities of LMICs, we can make significant strides toward reducing the radiotherapy gap and improving cancer care outcomes globally. Enablers of safe adoption of hypofractionated techniques in resource constrained regions include enforcement of stringent quality assurance protocols, proficient and adequate workforce, and maintenance of equipment.

Section 3: Access to theranostics: projections for ^{177}Lu-PSMA use, costs and social impact

Projections for ^{177}Lu-PSMA utilisation globally

The use of ^{131}I treatment for the treatment of hyperthyroidism and thyroid cancer has been established as part of standard of care for more than 50 years, is widely available and the most commonly used radionuclide treatment across the world (Table 1, Figure 5).[3,4] While the treatment of bone pain, neuroendocrine tumours and liver cancer have emerged as highly effective therapies and resulted in regulatory approval in many countries, the recent approval of ^{177}Lu-PSMA for the treatment of metastatic castrate-resistant prostate cancer by the FDA and EMA, based on pivotal phase II/III trials, has highlighted the challenges of implementing new theranostic treatments in many countries and for larger patient populations (Table 1, Figure 8).[3,4,70-72] The current availability of ^{177}Lu-PSMA treatment is limited to mainly high-income countries, and issues relating to workforce and funding have emerged as major factors in more widespread availability.[3,4,43,51]

To calculate the global eligible patient population for ^{177}Lu-PSMA therapy, based on current FDA and EMA approvals, and projecting the necessary doses required per year, we collated 3-year prostate cancer prevalence data for each country from the 2022 GLOBOCAN database, an online resource developed by the International Association of Cancer Registries.[27] Utilising prevalence rather than incidence allowed for a focus on the disease's prevalence in later stages, where patients could potentially benefit from ^{177}Lu-PSMA therapy. Countries lacking prevalence data were excluded from the analysis to ensure accuracy. Subsequently, the prevalence of stage IV cancer patients was calculated, with 18% reported for high-income countries, and 42.9% for middle and low-income countries.[73-75] This discrepancy potentially indicates a higher prevalence of advanced-stage disease at diagnosis in lower-income countries, consistent with observed mortality rates.[76] We assumed that almost all Stage IV patients may eventually develop castration-resistant metastatic prostate cancer, an estimation supported by existing literature.[77] While it is recognised that duration of response to androgen deprivation therapy can vary, in the majority of patients they will develop disease progression. Sequential treatment eligibility was then assessed following National Institute of Care and Excellence (NICE) guidance, with 35% of metastatic castration-resistant prostate cancer patients deemed suitable for docetaxel, among whom 55% were considered eligible for second-line chemotherapy.[78] Based on VISION trial criteria, it was assumed that 90% of calculated patients would meet the criteria for ^{177}Lu-PSMA therapy.[71] Furthermore, we estimated a 50% response rate to ^{177}Lu-PSMA therapy. To calculate the required number of vials, it was assumed that responders would necessitate five vials, while non-responders would require two vials, as established by prior research findings.[79]

Based on these data and assumptions, the number of patients eligible for ^{177}Lu-PSMA therapy is estimated to be more than 158,000 per year, and total number of doses of ^{177}Lu-PSMA required per year is more than 553,000 (Table 5). The number of potentially eligible patients for ^{177}Lu-PSMA therapy is greatest in high income countries (56.7 per million), which is double that of upper-middle income countries (24.6 per million) and 10 times that for lower-middle and low income countries (5.5 and 3.5 per million) which aligns with the higher prevalence of prostate cancer diagnoses and related to effective screening programs in those countries (Table 5, Figure 13). The availability of standard of care treatment for metastatic prostate cancer in LMICs may also impact on suitability of patients for ^{177}Lu-PSMA treatment. The numbers of eligible patients are in marked contrast to the current availability of ^{177}Lu-PSMA treatment in many LMIC, as well as HIC, highlighting the gap in need versus availability (Table 5, Figure 10). In view of the projected doubling of diagnoses of prostate cancer by 2040, the numbers of patients eligible for ^{177}Lu-PSMA treatment are likely to increase further.[80] The possibility of having future approvals for ^{177}Lu-PSMA therapy earlier in the treatment of patients with metastatic prostate cancer would also increase the numbers of patients suitable for treatment.[4] In addition to issues of sufficient sites in each country to deliver these theranostics treatments, an adequate trained workforce, and funding necessary for implementation, the supply of ^{177}Lu may also be an issue in view of the current and projected production from suitable reactors.[54] Calculations of the current global capacity of reactor production of ^{177}Lu has been estimated to be around 7.5 PBq (204 kCi) per year, which would provide treatment for approximately 150,000 – 180,000 patients per year. This may increase to 23 PBq (612 kCi) per year by 2032 based on new reactor production capacity being available, and new technologies for ^{177}Lu production may also enable greater supply which will be necessary to supply the global demand for theranostics use.[54]

^{177}Lu-PSMA costs and social impact

To evaluate the costs and social impact of ^{177}Lu-PSMA treatment, we evaluated the costs as well as the social impact initiated due to the usage of radiopharmaceutical therapy compared to the Standard of Care (SoC) in metastatic castration-resistant prostate cancer (mCRPC) patients in nine countries (Australia, Germany, India, Jordan, the Netherlands, the Philippines, South Africa, Thailand, and the United States) over the years 2023 to 2029. We considered two scenarios. In the first scenario, we estimated the effects that could occur if all patients eligible for ^{177}Lu-PSMA would receive the treatment. In the second scenario, we assumed a proportion of 10% of eligible patients currently receiving the treatment, thus representing the real-world number of patients.

A stepwise approach was used to define the number of patients eligible for ^{177}Lu-PSMA treatment. In the first step, we determined the number of patients with prostate cancer based on the annual incidence and population forecast. In the second step, we estimated the proportion of patients with prostate cancer who developed mCRPC. We considered regional variance between high-income (Australia, Germany, the Netherlands, United States) and upper-middle income (India, South Africa, Thailand) and lower-middle income (Jordan, Philippines) countries, resulting in 18% of prostate cancer patients developing metastatic prostate cancer in high-income and 42.9% in middle-income countries.[75-75] In the third step, we determined patients suitable for docetaxel (35%), subsequently estimated the proportion of patients that could be considered for second-line chemotherapy (^{177}Lu-PSMA population) (55%), and in the last step applied the rate of patients suitable for Lu-PSMA, based on positive PSMA scans in patients screened in the VISION study (90%).[71,78]

To determine the costs, we assumed five cycles of ^{177}Lu-PSMA therapy for patients who responded to treatment and a 50% response rate, with non-responders receiving two cycles of treatment.[79] Cost data was retrieved from publicly available sources or information obtained from Institutions in countries (Supplementary data). The cost range for all considered countries is between 1,880 USD in

India and 240,297 USD in the United States for five treatment cycles. The variance between the countries is also underlined in the context of the GDP per capita figures in 2024 in relation to the treatment costs (Figure 14). While treatment in Australia amounts to 0.43 of GDP per capita, this ratio increases to 15.08 in the Philippines. The data underlines that the costs in the context of the GDP per capita are higher in low-income countries, ranging from 5.06 in South Africa to 15.08 in the Philippines. The only exception is India, which has a ratio of 0.63, which is close to the ratio in Australia.

The economic benefit of ^{177}Lu-PSMA therapy was quantified by calculating the social impact. By applying the human capital approach for paid work, we value the economic contribution to the gross domestic product (GDP) through the quality adjusted life years gained. Every paid productive activity within an economy is accompanied by the consumption of goods and services from intermediate suppliers. Economic activities, therefore, result in further activities and the creation of gross value added (indirect and induced effects). Beyond the direct, indirect, and induced effects of employees' economic activity on the labour market, we also consider unpaid work, the value of non-market activities such as household production and voluntary work. These effects are not captured in National Accounting systems. By capturing this value "beyond" GDP, we acknowledge the contribution of those activities to a nation's wealth by both employees and the non-working population. Therefore, the economic benefits cover different categories: paid direct, paid indirect, paid induced, and unpaid indirect and sum up to the social impact. By quantifying health impact spillover effects along the supply chain (direct, indirect, and induced value-added effects) and including unpaid work, we take a broader societal perspective and aim to capture health intervention's value for a society beyond the clinical scope.

We followed three main steps to determine the social impact. In the first step, we determined the incremental health benefits of ^{177}Lu-PSMA therapy compared to the Standard of Care (SoC) in the range of the determined patient populations. In the second step, we translated the incremental benefit into avoided productivity losses in terms of paid and unpaid work. Thirdly, we monetized these avoided productivity losses (Supplementary data). The social impact generated was calculated for a scenario in which all eligible patients (EP) who would receive radiopharmaceutical therapy and for the assumed real-world patients (RWP) (Supplementary data). The differences between those two scenarios depict the foregone potential of social impact that could be generated if all eligible patients receive the treatment in Australia, Germany, India, Jordan, the Netherlands, the Philippines, South Africa, Thailand, and the United States over the years 2023 to 2029.

This analysis showed that Australia is expected to experience a foregone social impact of approximately $40.39 million over the period, starting from $5.31 million in 2023 and increasing to between $6.39 million by 2029. Germany's figures are notably higher, with the impact estimated $72.05 million throughout the period. The annual estimates rise from $9.33 million in 2023 to $11.09 million by the end of the period. India shows a lower foregone social impact with $6.50. However, the growth potential is evident, with the figures growing from $0.72 million to $1.16 million by 2029, highlighting the need for timely and effective interventions. Jordan, displaying the most petite figures, could see an impact of $96 thousand, with annual figures marginally increasing from $11 thousand in 2023 to almost $16 thousand in 2029. The Netherlands anticipates an accumulated impact of $13.37 million, with annual estimates from $1.71 million in 2023 to nearly $2.1 million in 2029. The Philippines estimates accumulate to almost $1.3 million over the seven years, beginning with $145 thousand in 2023 and escalating to $231 thousand by 2029. South Africa expects a cumulative impact of $6.90 million, with 2023 estimates of almost $1 million. This cumulative impact underscores the magnitude of the issue and the need for comprehensive solutions, rising to almost $1.06 million by the end of the period. Thailand could see a total foregone social impact of $3.16 million, with the annual figures starting at almost $400 thousand in 2023 and reaching almost $528 thousand by 2029. The United States predicts the most substantial impact, with total estimates of $580.45 million. The annual impact in 2023 is expected to be $74.51 million, increasing to $92.35 million by 2029.

These nine countries collectively anticipate a foregone social impact totalling $725 million over seven years. This analysis quantifies the foregone social impact and underscores the significant disparities in unrealized treatment potential across different national contexts, emphasizing the urgent need for action and the broad spectrum of socio-economic impacts associated with health interventions.

Section 4: Radiation protection, safety and quality systems

Radiotherapy

Quality and safety are crucial aspects for establishing and maintaining best practice and optimizing outcomes in radiotherapy. They rely on the implementation of a quality management system that embraces essential components of the clinical framework including processes, technology, and human resources. Without a proper quality management system in place, the risk of radiotherapy treatment misadministration and the likelihood of less accurate treatment delivery is greater.

Radiation protection and safety in medical uses of ionizing radiation encompass the protection of not only workers, such as the health professionals delivering the radiotherapy, and the public, who are shielded from the radiation in the imaging and treatment rooms, but also the patients, who are protected from unnecessary and unintended exposures to radiation.[81] Fundamental for the safe use of radiation in medicine is the implementation of safety standards, notably the IAEA Safety Standards for this area, providing the principles, requirements and recommendations to ensure safety, including at both national and facility level.[82,83]

Quality management

Quality management requires dedicated resources, adequate facility infrastructure, systematic activities and programs to be implemented. These must be planned and budgeted whenever a new radiotherapy program is established, or an existing one is upgraded to more advanced techniques and capabilities or expanded to include more treatment modalities and equipment. A reliable infrastructure includes electricity supply, and opportunities for use of solar energy and renewable sources of electricity is an important consideration. A multidisciplinary team of radiotherapy professionals, including radiation oncologists, medical physicists and radiation therapists are generally needed to establish a quality management system, essential for safe and effective operation of the radiotherapy departments globally, in lower- and middle-income as well as high-income countries.

Technology permeates the entire clinical radiotherapy process with imaging and treatment delivery equipment, ancillary devices, software for patient management (oncology information system), including features for treatment record and verify, and for treatment plan calculation. Safe and effective use of each technological element is critical in achieving quality delivery of radiotherapy treatments. Adequate resources should therefore be allocated to "monitoring all aspects of the functional performance of radiotherapy equipment by comparing parameters against tolerances set at strict but achievable values".[84] This quality assurance (QA) program provides adequate confidence that the involved equipment and software meet the expected requirements for quality and the risk of inaccurate treatment delivery because sub-optimal functional performance is minimized. Guidelines published by professional organisations are available to support the clinical staff in performing QA. Clinically qualified medical physicists have a central role, as they are responsible for the development and implementation of the physical and technical details of the QA programs.[85] There are various levels of complexity and frequency of QA procedures and additional equipment, such as QA phantom and dosimetry devices, is needed. Of note, more advanced radiotherapy techniques require more intensive QA procedures performed with more sophisticated QA equipment.

Equipment and software QA are necessary but not sufficient for ensuring safety and quality in radiotherapy. Well established clinical workflows and processes play a crucial role, as they define how the equipment is used by the involved health professionals. Safety procedures, clinical and QA protocols, and standard operating procedures are all included in the quality management system of a radiotherapy infrastructure. Risk-based analysis methods can be applied to improve workflows and processes in order to enhance the safety and quality of radiotherapy treatments.

Instilling a radiation safety culture into the healthcare setting is of great importance for ensuring the safety of the patients, workers and the public. Part of this is the effective safety learning in the organization and by the health professionals therein. Safety learning is aided by Incident Learning Systems (ILS) designed to capture unsafe conditions, near misses and incidents to enable action, and improve communication, response and learning. The IAEA provides an ILS for therapeutic medical radiation uses.[86] The Safety in Radiation Oncology (SAFRON) was launched in 2012, as a non-punitive integrated voluntary reporting and learning system.[87] A total of 1685 reports had been submitted into the SAFRON system from its inception until 2021. Analyses of 501 cases in which the cause of incident was identified, revealed that the most common cause of incident was related to the inadequate communication, followed by lack of adherence to the standard procedures and practice, miscommunication, inadequate documentation in planning, lack of communication, etc. Most of the incidents (75 %) were considered to be minor incidents while only 1% of all reported incidents were considered to be critical. Analysis has shown that communication problems and failure to follow standards, procedures, or practices, are the most frequent causes of radiotherapy learning events.[87] Safety barriers are an important concept in risk management. The SAFRON report analysis demonstrated that, in many cases, a combination of two or more safety barriers can be effective in identifying incidents.[87] Regular independent chart checks and intra-treatment monitoring were the safety barriers that most frequently identified incidents, whereas in vivo dosimetry and patient ID verification were the least frequent.

It is important to also note that radiotherapy should be context specific, and some LMICs may not be able to support advanced radiotherapy services but would need context appropriate machines or interventions. In addition, increased access to spare parts and better access to maintenance, including preventive maintenance would also be helpful in improving health outcomes. Of course, LMICs have a wide spectrum of economic capabilities and infrastructure availability.

Professional staff

Radiotherapy requires an adequate number of competent professional staff to ensure that quality treatments are safely delivered to the patients. Staff should have received the proper education and training and should undergo continuous professional development to improve their professional skills and keep their professional knowledge updated. Certification of their professional competences through successful completion of accredited training programs is a pre-requisite. Staffing needs depend on the provided services. Introduction of new treatment techniques and modalities should always be accompanied by adequate staffing levels and competencies adaptation. If institutions are actively involved in education and training programs, staffing levels should be adapted accordingly. Staffing levels are also frequently specified for practice accreditation purposes and professional credentialing.[88] The lack of qualified professionals as a consequence of lack of available education and training program is frequently an issue for less resourced countries. A critical mass of accessible infrastructures and experienced qualified staff is usually needed to establish a virtuous circle at a national level. International support is otherwise needed.

Audits

As part of a comprehensive approach to QA in radiotherapy, independent external audit is essential to ensure quality of practice and treatment delivery. The audits can vary in type and scope, either addressing specific part of the radiotherapy process or assessing the entire process in the form of comprehensive audit.[89,90] audits play a fundamental role in assuring and improving quality patient care. Independent dosimetry audits, as an example of partial audits, are an effective way to verify whether the quality of dosimetry practices at a radiotherapy centre are adequate to achieve cancer treatment objectives. Dosimetry audits assist in identifying problems and provide support in their resolution, contribute to accuracy and consistency of dosimetry and good medical physics practices.

In some cases, audits are used for accreditation purposes and licensing of radiotherapy programmes. Several organisations worldwide provide different levels of radiotherapy audit services. IAEA has a long history of providing assistance for dosimetry audits to its Member States. Together with the WHO, since 1969 it has operated postal dose audit programme to verify calibration of radiotherapy beams. The experience suggests that basic audits of the beam output in the reference conditions should be mandatory for all radiotherapy centres to ensure that beams used for patient treatments are correctly calibrated, whereas more advanced audits should be usually offered for new technologies in radiation oncology.[91] With 17,408 beam checks conducted in 2,649 hospitals across 144 countries, the programme managed to improve accuracy of radiotherapy treatments over the last half of century. (Figure 15).[92] Furthermore, IAEA has developed a set of procedures for experts undertaking missions to radiotherapy departments for the on-site review of dosimetry equipment, data, techniques and measurements, and education programmes for local staff. This methodology involves dosimetry and medical radiation physics aspects of the radiotherapy process without assessing clinical areas. Since 2007, comprehensive clinical audits under the Quality Assurance Team for Radiation Oncology (QUATRO) framework has been successfully applied in numerous clinical audits worldwide

Radiotherapy quality can also be assessed through cancer specific national audit programs. For example, the UK national prostate cancer audit developed the first outcomes reporting program for radiotherapy, publishing treatment complication rates, patient reported outcomes (PROMs) and patient experience measures (PREMs) across all public sector hospitals to support quality improvement.[93] Further work in LMICs has sought to develop a priority set of quality indicators for cancer care across all resource settings which includes specific radiotherapy performance indicators.[94]

Theranostics: quality and safety

The framework of nuclear medicine integrates detailed regulatory guidelines globally, crafted by national and international bodies. These guidelines cover facility operations, radiopharmaceuticals handling, and professional training, adapting to technological advancements and interdisciplinary intersections.[43,51,54-56] Collaboration with organizations and agencies ensures worldwide standardisation. Audits are key in maintaining compliance and quality. The IAEA's contributions include basic safety standards, guides for professionals, and aligning practices with current research and ethics.[55,56] Despite regional variations, entities such as EANM, SNMMI, ANZSNM and IAEA guide the establishment of theranostics centers, fostering global cooperation and compliance with safety regulations.

Advancements in nuclear medicine imaging, like SPECT and PET scanners, have revolutionised diagnostics and treatment monitoring, offering detailed cellular and molecular insights.[3,4,6] These systems provide vital information for patient care, relying on regular maintenance, calibration, and software updates for accuracy. Standardisation, essential for consistent global results, is supported by programs like the SNMMI, EARL and ARTnet accreditation for PET and SPECT scanners, and international protocols by bodies like the IAEA. Collaboration across healthcare stakeholders and attention to patient history are crucial for maximizing clinical benefits from these advanced imaging technologies.[48,55]

Dosimetry, which is essential in nuclear medicine and radiation therapies, faces challenges despite advancements in software and technology. These tools, which refine radiation dose calculation and side effect prediction, aim for precision and patient-specific data.[3,4] However, integrating data across different systems, adapting to new imaging and therapy technologies, and developing real-time solutions are key challenges. Collaboration among researchers, clinicians, and industry is vital for standardising protocols and leveraging AI for data analysis. Training and education are crucial for professionals to navigate these complexities.[3,4,6] The goal is to maximize therapeutic potential while ensuring patient safety, a challenge met with ongoing research and a commitment to excellence.

Clinical audits also play a role in evaluating the implementation of standards and guidelines.[55] The value of dosimetry in achieving more optimal dosing in nuclear medicine theranostics cannot be overstated. By enabling precise measurement of absorbed radiation doses, dosimetry ensures that therapeutic radiopharmaceuticals deliver the maximum possible dose to tumours while minimizing exposure to healthy tissues. This personalized approach enhances treatment efficacy and reduces the risk of adverse effects.[6] As expertise in dosimetry grows, the practice will become more widespread, leading to improved safety and therapeutic outcomes. The integration of advanced imaging techniques and AI-driven analysis will further refine dosimetric calculations, making it possible to tailor treatments to individual patient needs with unprecedented accuracy. This evolution promises to elevate the standard of care in nuclear medicine theranostics, ensuring optimal efficacy and patient safety.[55]

Accreditation in nuclear medicine signifies quality, safety, and excellence, enhancing trust among patients and professionals. It involves evaluations, audits, and adherence to international standards.[52,55] Globalisation facilitates the exchange of research, methodologies, and technologies, which are crucial for the field's advancement. Standardisation is vital, ensuring consistent quality of care worldwide. Continuous education and training are essential for professionals to keep pace with rapid advancements. The future of nuclear medicine, which integrates technology and biology, offers promising diagnostic and therapeutic possibilities. This progress requires global collaboration, a commitment to excellence, and a focus on patient-centric care. While accreditation marks a milestone, continuing education, ongoing collaboration and innovation are key to fully realizing nuclear medicine's potential.

Section 5: The potential for advances in digital sciences for improving cancer care in LMICs

Advances in digital sciences, and their integration with multimedia devices (e.g., smartphones), have crucial roles to play in expanding and improving healthcare in LMICs. The term “digital health” has been defined as “encompassing electronically captured data, along with technical and communications infrastructure and applications in the health care ecosystem”.[95] Examples of digital health applications include---but are not limited to--telemedicine, the digital capture and display of health information, knowledge integration (e.g., using decision aids, predictive analytics, and artificial learning/machine learning), diagnostics (onsite and remote), and the use of implantable devices for tracking, monitoring and triggering.[6,96] Making digital health technologies accessible to both healthcare practitioners and patients can improve equity in healthcare.

Major advances in telemedicine capabilities have made it possible to provide higher-quality healthcare, including cancer imaging and therapy, particularly for patients in remote or underserved areas.[6] Telemedicine empowers patients to consult with healthcare providers through virtual platforms using computers or mobile phones, for example. Live video visits and remote patient monitoring not only offer convenience but, crucially, increase access to medical specialists by reducing the need for travel. They can facilitate the triage of patients to urgent or emergency care facilities and help direct patients to the appropriate physicians in a timely manner. This has relevance to both the delivery of radiotherapy and the treatment of patients with theranostics, where patient review and follow-up are required throughout the treatment journey. The adoption of electronic health records, made available to physicians and patients, further facilitates quality and safety in both in-person and remote healthcare delivery by increasing the efficiency of care coordination, reducing duplication of orders, and improving communication with patients.[6] While telehealth has numerous benefits, particularly for patients in difficult-to-access areas, local medical providers play important roles for patients. These community healthcare workers can conduct day-to-day oversight of patient care. Importantly, digital health technologies can bridge specialists not only with patients but also with their local providers.

Multimedia, artificial intelligence and virtual reality - digital technologies for the delivery of education of health practitioners and patients

Digital technologies can also substantially improve access to education for healthcare trainees and practicing providers. For example, these technologies can broaden access to continuing education, allowing more providers to stay up to date on the latest advances in healthcare.[6] Digital technologies can enhance the education of patients as well, for example by providing them with instructional videos on their disease, its natural history and treatment, and what to expect during treatment. Multimedia communication approaches can reach patients with different learning styles by providing educational materials in diverse, interactive formats. They can also provide educational materials tailored for patients with different levels of education, cultural backgrounds, and native languages, making healthcare interactions more comfortable. The use of multimedia technologies has been found to improve patient satisfaction, engagement, and quality of life and reduce healthcare costs.[6]

Training and education are pivotal to expanding workforce capacity in radiation oncology and nuclear medicine, and to ensure the quality of care. The urgent need for education and training solutions has been particularly acute in the LMIC setting due to workforce needs and the changing technologies utilised.[51,97] In radiotherapy, the greater accuracy of CT-based treatment delivery offers improvements in survival (dose escalation), reductions in morbidity (due to organ sparing) and greater efficiency (through hypofractionation).[98] The lack of workforce for theranostics implementation has also been shown across the spectrum of clinical and scientific areas in both HI and LMIC.[51-53]

The rapid integration of Artificial Intelligence (AI) into healthcare systems is offering unprecedented opportunities for improved diagnostics, treatment planning, and patient care, as well as to potentially ameliorate the workforce shortage. For radiation oncology, one option is using AI to automate critical quality processes and support clinical processes; in nuclear medicine imaging, AI can be used to enhance diagnostic accuracy and treatment monitoring by automating data analysis, improving image reconstruction, and identifying patterns that may be missed by human operators, thereby maximizing the clinical benefits of advanced technologies like SPECT and PET scanners.[6,99]

While bringing potential benefits to healthcare, the application of AI systems also introduces new challenges and risks.[100]The integration of AI systems in clinical settings is currently hampered by limited generalisability in different populations, fragility in real-world scenarios, and lack of transparency. However, since this is a rapidly evolving field, a wider availability and adoption of AI-based tools to support many processes is expected in the near future.[101]

In a resource-stratified context, there is an urgent need to ensure practitioners within the radiation oncology and nuclear medicine workforce are equipped with the necessary skills to utilise and assure the quality of the increasing scope of technical innovations.[102,103]
Guidance has been provided by the IAEA and the European Federation of Organisations for Medical Physics for academic modules, clinical training programs, and/or continuous professional development activities for in the field of AI for medical physicists.[104] The growing gap between HI and LMIC in technical expertise has made the need to bridge the education and training gaps more acute.[105] The challenge is how to deliver accredited training where expertise may be scarce or difficult to access.

The widespread availability of internet access globally, even in the lowest-income settings, has provided the opportunity for delivery of online (E-learning) and tele-education tools for high-quality workforce development.[106] This includes multidisciplinary training networks delivering radiation oncology curricula and brachytherapy expertise, hybrid teaching (didactic, hands-on, asynchronous) utilising the Project ECHO (Extension for Community Health Care Outcomes) model or offering continuous medical education through virtual Chart Rounds and case discussions focused on disease sites or technique. [107-111] Whilst a number of these initiatives are based on international collaboration (Global North to Global South), there is good evidence from China of how rapid expansion of radiotherapy workforce capacity and training can be achieved, particularly in rural areas, through a tele-radiotherapy system.[112] Web-based training tools are also being used for centres to support participation in studies and trials of new radiation technologies and techniques (e.g., stereotactic radiotherapy) to ensure centres are quality assured and able to participate in an efficient manner.[113] Similar programs for theranostics training and for patient information are also being developed by IAEA and not-for-profit organisations.[114]

One of the key questions around e-learning is whether it remains as effective as face-to-face teaching delivery. Studies have broadly demonstrated that e-learning and web-based tools are associated with high satisfaction and knowledge levels, and improvements in contouring for radiation oncology.[113-115] In addition, web-based solutions provide better reach geographically to more rural or remote areas within individual countries or internationally, but this needs to be balanced with lower levels of compliance. The online platform, Advanced Medical Physics Learning Environment (AMPLE) is an example of an online tool designed to support building medical physics capacities in Asia and the Pacific.[116] This IAEA-developed environment provides medical physicists with guided learning materials and remote mentorships to enhance their clinical training in hospitals. Moving forward there is now increasing attention to the interactivity/fidelity of online training modules, and how they support the user experience, knowledge translation and quality improvement.[117,118]

Radiotherapy contouring/target volume delineation (TVD) has been identified as a critical area for training and is a key component of curricula. In addition to online teaching courses, a number of open-source information communication technology (ICT) platforms have been tested and have demonstrated improvements in the quality of target delineation in radiation oncology—for example, e-contour and FIELD-RT.[119,120] EduCase, another web-based platform, has been shown to be effective when dovetailing with interactive, focused face-to-face workshops.[121] For medical physicists, and RTTs, Virtual Environment for Radiotherapy Training (VERT) is an interactive platform simulating linear accelerators, plans and treatment delivery which has been used successfully in medical education programs.[122] Further innovations using virtual reality (VR) can re-create the complete radiation oncology clinical environment and have been used, for instance, to support training in patient positioning as well as other processes within the radiation therapy workflow.[123]

Role of digital health technologies in advancing medical research and the development of clinical practice guidelines in LMIC

Despite many challenges in implementing digital technologies in LMICs, digital sciences are vital for improving not only healthcare practice but also healthcare research in LMICs. By enabling the collection and analysis of large datasets from LMIC, digital technologies will strengthen approaches for cancer prevention and provide new insights into effective treatments.

The use of digital sciences was recommended in “Medical Imaging and Nuclear Medicine: A Lancet Oncology Commission,” as it was found to be important for education and enhancing access and availability of expertise in imaging in LMIC.[6] Use of digital sciences may enable and encourage greater ownership of contextual cancer research in LMIC, which in turn may help to address the fact that by 2030, approximately three-quarters of all cancer deaths will occur in LMICs.[124,125] Only 8% of global phase 3 clinical trials conducted between 2014 and 2017 were led by LMICs, less than a third of registered clinical trials for the three highest-burden cancers enrolled patients from LMICs in the period from 2010 to 2017, and many countries in sub-Saharan Africa recorded no cancer clinical trial activity during this period.[124,126-128]

More generally the evidence points to limited infrastructure and capability for clinical trials in both HIC and LMIC. Primary analysis of research publications on radiotherapy has demonstrated that only 5% of research outputs in radiation oncology are related to clinical trials, and that this figure has remained constant since 2000 (Aggarwal, A., unpublished data, September 2023). Notably, the ratio of phase 3 to phase 2 studies has been steadily decreasing over the last decade. This is suggestive of potential concerns regarding costs and infrastructure requirements of delivering large phase 3 studies and also the low regulatory bar for the adoption of new technologies and techniques indicating an increasing preponderance of phase 1 and 2 studies and case series data. With respect to randomised clinical trial (RCT) output among LMICs, India has been a notable exception over the last decade, showing a strong commitment to phase 3 clinical trial research.

Despite outputs increasing over time in LMIC, the impact of the research done in LMIC as defined by citations remains well behind that of work done in HI, and this circumstance ultimately influences clinical practice guidelines.[129] There is also a disconnect between clinical trial activity and global burden of disease. The major disease sites undergoing RCT evaluation include breast, prostate, head and neck and lung. However, high-burden tumors such as cervix and hepatocellular cancers have been the subject of limited trial evaluation.[130] Given that one of the aims of this report is to contribute to multilateral cooperation and integration, we reaffirm research priorities for LMICs for the next decade and highlight the value creation made possible by digital sciences (Table 6).[124]

Keys to implementation and adoption of new digital health technologies in LMIC

While the implementation of new technologies to improve healthcare access and equity is important in all countries, it plays a particularly important role in LMIC. Given the limited resources available, judicious development and adoption of these technologies is critical. Studies are ongoing in this regard. For example, the ARCHERY study is a prospective international multicentre study assessing the quality and cost efficacy of a web-based AI tool for contouring and planning across India, South Africa, Malaysia and Jordan and will report in 2026.[131] Education on how to access and use these technologies will be critical in their widespread adoption by patients and practitioners. Furthermore, success depends on strong partnerships and co-evolution of technologies between key players in government and healthcare, including hospital systems and insurance companies. Barriers between different health systems need to be removed to share patient health information and facilitate consultation and treatment by providers who may be in remote locations. Meanwhile, protections need to be erected to ensure privacy of health information, defend against cyberattacks, and prevent discrimination against vulnerable populations. The cybersecurity framework developed by the United States National Institute of Standards and Technology could serve as a guideline.[132]

Section 6: Challenges and lessons learned – Radiotherapy global access

The Lancet Oncology Commission report on expanding global access to radiotherapy in 2015[2] included a call to action consisting of 5 actions. The first action was to incorporate radiotherapy into population-based plans in 80% of countries by 2020. However, after an analysis of 2018 data performed in 2021, it became clear that significant efforts are still needed to highlight the importance of achieving this goal. Only 55% of 143 countries with available data on National Cancer Control Plans (NCCP) included radiotherapy-related items. The likelihood of receiving radiotherapy in the NCCP was correlated with number of machines, income level and region, with low-income level and Asia Pacific region having an even lower rate.[133]

The second action called for the expansion of access to radiotherapy, aiming for an increase of 25% in treatment capacity and creating at least one cancer centre in each LI and LMIC. While there has been an increase in the number of machines world-wide, the number of cancer cases have increased as well, and comparison of 2013 versus 2022 radiotherapy machine data in DIRAC showed either stable or increased number of radiotherapy machines in all but 5 countries. The number of machines increased from 13,103 to 15, 460 machines in that time period which represented a 18% increase in machines. The number of machines per million population increased in 13/15 regions globally. For example in Africa alone, of 52 African countries only 23 had teletherapy in 2010. By March 2020, 28 of 54 countries had access to external beam radiotherapy, still leaving a considerable gap.[29,30,133] This conundrum highlights the importance of using the existing machines more efficiently and developing innovative solutions to increase access and efficiencies such as through hypofractionation and automation.[29,30,133] [1] Real life scenarios that affect access include challenges associated with distance from radiotherapy facilities. Financial support and/or provision of transport options and patient lodging are needed.

The third action was human resources for radiotherapy. Evaluation of progress for the third call to action is very complex, since numbers of radiotherapy workforce may represent an increase due to education and training, one must also take into account attrition, whether voluntary or involuntary due to socio-political, economical and other reasons. Furthermore, proxy metrics, such as number of national training programmes, are not routinely reported and collected at global levels. LMICs are particularly affected by the shortage in human capacity.[134,135] In terms of absolute numbers, focusing for instance on the region covered by the Asia Oceania Federation of Organisations for Medical Physics (AFOMP), a recent study projected a need for almost 6000 additional radiotherapy medical physicists across 21 countries in the region, provided that the required number of teletherapy machines was installed.[134] Nevertheless, the recognition of medical physicists as health professionals represents a significant challenge in several countries, particularly LMICs. The IAEA, in collaboration with some regional professional organizations, recently collected information on the main issues faced by medical physicists at a professional level. It emerged that the lack of recognition impedes the advancement of the profession, "with challenges such as a shortage of clinically qualified medical physicists, inadequate education and training programs, limited enforcement of regulations, bureaucratic processes, and limited advocacy efforts". In terms of education and training, according to the IOMP survey 84.4% of the respondents from medical physics organizations have university-based medical physics courses and 68.7% have official clinical medical physics training programmes.[135] Availability and duration of training programs show significant differences across regions. Significant differences are observed across regions in terms of the availability and duration of the training programs. Collaborative efforts between the IAEA, professional organisations, and stakeholders are needed to achieve progresses in recognition, access to and harmonisation of education and training resources. In addition, modification and innovation in training programs is urgently needed, in addition to expansion of the number of training slots. Initiatives such as Rays of Hope[136], and the Cancer Moonshot 2.0, aim to assist resource-challenged countries in establishing or expanding their capacities in radiotherapy, radiology, and nuclear medicine. The expansion of training will be addressed partially though IAEA support of Rays of Hope Anchor Centres. Of course, the Rays of Hope initiative consists of not only a pillar for development of radiotherapy and diagnostic imaging centres and training of personnel for these, but also includes 2 other pillars. The second pillar is Anchor centres that will enhance South to South collaboration and support and the third pillar of innovation which includes a global database and image repository (Sunrise initiative) nand innovation in education and treatment.[136]

The fourth action was sustainable financing to expand access to radiotherapy, and the increase in interest in funding radiotherapy by various entities such as development banks such as Islamic Development Bank, African Development Bank, Asian Development Bank and others reflecting a greater recognition of the essential nature of radiotherapy as a pillar for cancer treatment from cure to palliation. For example, in 2022, a linac and a brachytherapy machine were procured using funds provided to the IAEA by Niger as part of an Islamic Development Bank (IsDB) loan to Niger, to support the expansion of radiotherapy services in Niger within the Rays of Hope initiative. (Ref: gc67-inf5.pdf (iaea.org) While specific data is not available, requests for the IAEA to support these funded activities in countries have increased significantly. The ensuing collaborative partnerships with the IAEA to support radiotherapy access are evident through partnerships in Rays of Hope and other activities.[136] In addition, public private partnerships may contribute to partially addressing the access gap if accompanied with agreements with the government to ensure that the general population has access to care through such initiatives.

Action 5 is to align radiotherapy access with universal health coverage. Comprehensive understanding of progress on this action needs assessment of inclusion of radiotherapy in cancer benefit packages beyond tracer cancers (cervical, breast and lung). The WHO reported on Health Benefit Packages (HBP) and the extent to which radiotherapy is included in the UHC (Figure 16).[137] Radiotherapy was the cancer treatment modality that varied most between country income groups, with a four-fold difference in coverage between HI and LIC in the public-sector Health Benefit Packages (HBP). Lung cancer radiotherapy coverage showed the greatest difference. For example, in LMICs, a quarter of the HBPs that covered breast or cervical radiation did not include lung radiation. Overall, basic radiotherapy was included in 69% of HBPs for cervical cancer, 67% for breast cancer and 62% for lung cancer and varied by region and country. So far, the WHO report on inclusion of cancer care in health benefit packages is the only globally available evidence with data benchmarked in 2020-2021. Future follow-up of the report at later timepoints can provide quantitative estimates of progress.

Section 7: Research and innovation

Radiotherapy

Exciting areas of research and new directions in radiotherapy were highlighted recently, yet the lack of sufficient resources to support research was also noted as an obstacle to continued evolution of novel treatments.[138] A recent review identified several key areas of innovation in radiotherapy. Hypofractionation, delivering high doses of radiotherapy in a few sessions, can reduce treatment time and costs while maintaining efficacy in cancers such as prostate, breast, and lung. Resource-sparing oncology research and radiotherapy as virtual surgery show promise, with radiotherapy being a low-cost, non-invasive alternative to surgery for certain cancers. Extreme hypofractionation and radiation for oligometastatic disease could offer long-lasting remission and fewer systemic treatments. AI in radiation oncology can improve image reconstruction, segmentation, treatment planning, and toxicity prediction. Other notable advancements include functionally adaptive radiotherapy, real-time targeting, particle beam radiotherapy. Ultrahigh dose rate FLASH radiotherapy may show promise with less normal tissue damage than a conventional dose rate, while maintaining tumor response. Spatially fractionated radiotherapy, delivering heterogeneous doses, has shown promise in treating advanced and refractory tumors. Finally, combining radiotherapy with immunotherapy requires robust clinical studies to optimize strategies, particularly in low- and middle-income countries.[138] In addition, other types of research and innovation in education and training is also essential to the field in order to address the training gaps and needs. To support education and training in cancer care, the IAEA has developed virtual reality (VR) models for some cancer treatment procedures, using this technology as an innovative training tool for medical professionals worldwide.[138] First introduced in July 2023 during an IAEA training course in Mozambique with 180 participants across Africa, VR models aim to meet education and training needs in resource-limited settings, reducing knowledge gaps. The use of such VR tools is especially valuable in locations where equipment is unavailable or not yet operational.[139] These VR models will be integrated into the IAEA's comprehensive e-learning platform - Radiation Oncology Virtual Education Resource (ROVER), which is another excellent instrument in supporting the expansion of education and training among cancer care professionals worldwide. Developed by the IAEA, ROVER will allow access to a wide range of cost-free training materials, empowering health specialists with the knowledge and tools necessary to deliver optimal care to patients with cancer.[140] ROVER will significantly contribute to the existing training and will be particularly beneficial for the long-term fellowship training in the IAEA Rays of Hope Anchor Centres – regional leaders and centres of excellences in cancer care.

In addition, the IAEA works on a concept for a global radiotherapy database under the Rays of Hope. In April 2024, a multidisciplinary working group was established, comprising experts in radiotherapy, nuclear medicine, quality assurance, and medical physics. This group outlined a data collection framework and discussed system integration, capacity building, and data management, among other points. Research groups can facilitate capacity building, research training and the production of practice changing trials provided context appropriate research goals are driven by relevant stakeholders and avoid know ethical pitfalls. Examples include cooperative research groups such as the Radiation Therapy Oncology Group, NRG Oncology —and others such as the Southwest Oncology Group, Children's Oncology Group, and European Organisation for Research and Treatment of Cancer. Additionally, cancer specific Regional research groups such as the African Breast Cancer Study and the African Oesophageal Cancer Consortium enhance collaboration between HICs and LMICs. Another model is through regional Professional Groups such as the Federation of Asian Organizations for Radiation Oncology who have embarked on context specific multi-institutional international studies.[22]

Harmonized Data Standards and Digital Transformation

To enhance research and innovation in radiation medicine, the implementation of harmonized data standards is essential. Sharing information using a common language of data allows for more effective collaboration and integration across different institutions and countries. This standardization facilitates the aggregation and comparison of data, leading to more robust and reliable research outcomes. Additionally, the digital transformation from paper-based systems to paperless, electronic records is crucial for improving the quality of treatment. This shift enables the optimization of workflows, maximizes the use of advanced technologies, and ensures more precise and efficient patient care. By adopting harmonized data standards and embracing digital transformation, the field of radiation medicine can achieve significant advancements in research, clinical practice, and overall healthcare outcomes.

The IAEA's SUNRISE (Sustainable Unified Network for Radiation medicine Innovation and Scientific Excellence) project exemplifies this approach. As part of the Rays of Hope initiative, SUNRISE aims to develop a framework to evaluate the impact of radiation medicine across all levels of the health system. This harmonized data collection framework will facilitate the aggregation of data from numerous patients, enhancing research opportunities and driving improvements in cancer treatment, research, and education. By fostering global collaboration and integrating multidisciplinary inputs, SUNRISE will help optimize healthcare systems, enhance patient outcomes, and promote excellence in radiation medicine worldwide.

Virtual Clinical Trials (VCTs)

Virtual Clinical Trials (VCTs) in imaging offer a methodologically efficient alternative to traditional clinical trials for evaluating and optimising imaging technologies.[141,142] Virtual clinical trials (VCTs) in radiotherapy, particularly in stereotactic body radiotherapy (SBRT), offer a robust framework for simulating and optimizing treatment strategies. These trials leverage computational models to account for the complexities of tumour microenvironments, such as the heterogeneous oxygenation patterns within tumours. This approach circumvents the limitations of current in-vivo imaging technologies, enabling precise estimation of treatment outcomes and facilitating the design of more effective radiotherapy protocols.[143] VCTs have shown significant potential in optimizing treatment strategies for various cancers through outcome modelling and targeted therapies. In a study on outcome modelling using machine learning, a novel training technique called ExMixup was developed to predict treatment responses in patients with characteristics distinct from those included in past clinical trials. This approach demonstrated improved predictive performance, thereby enhancing personalised radiotherapy by identifying patient-specific doses that could reduce recurrence risks. [144] The use of VCTs in prospective radiotherapy trials will provide further evidence of this innovative approach to improved treatment outcomes.

Theranostics

The last decade has seen a marked expansion in the number of diagnostic and therapeutic radiopharmaceuticals entering clinical trials, leading to the development of evidence of clinical impact and the approvals of new imaging approaches in cancer patients.[3,4,6,43] In addition, the development of innovative radiochemistry approaches for the production of radiopharmaceuticals has led to widespread implementation in clinical trials across a broad range of cancer types.[43,54,56] These novel molecular imaging probes enable new insights into tumour biology, expression of targets suitable for therapy, prediction of response and potential toxicity, and allow selection of patients for new therapeutic radiopharmaceuticals.[3,4,6] The development of evidence for the use of diagnostic and therapeutic radiopharmaceuticals through multi-centre clinical trials, and including cost-effectiveness and patient reported outcome analysis, is being pursued by both academic and industry groups.[3,4,6,44,70] The number of new trials and companies pursuing new theranostic treatments has dramatically expanded over the last 5 years, and projections for new therapies continue to rise.[4,43]

The development of these new diagnostic and therapeutic radiopharmaceuticals has required the establishment of guidelines for production and quality control, as well as credentialling of sites and scanners used for imaging studies.[43,54,56] These have been proposed by a number of international organisations, including IAEA, SNMMI, EANM and ARTnet, and have established guidelines which facilitate the conduct of multi-centre clinical trials.[145,146] The generation of evidence from investigator-initiated studies for theranostic treatments has been quite successful, and aligns with industry-sponsored studies which have also been pivotal in regulatory approvals (eg VISION and TheraP trials for ^{177}Lu-PSMA).[70,71] Initiatives to extend these trial networks are currently being explored. This approach will continue into the future as further new theranostic approaches are pursued in large multi-centre prospective trials. By fostering a global network of research institutions and clinical centers, the nuclear medicine community can accelerate the development and adoption of theranostic technologies, ultimately improving patient outcomes and advancing the field of personalised medicine.

The development of prognostic and predictive imaging tools for new theranostic treatments continues to expand, particularly with the introduction of machine-learning and AI approaches to image analysis based on parameters established in prospective trials.[147-149] In conjunction with the further development of multi-centre trials exploring the evidence of management impact of new imaging probes, and health outcome improvements for novel theranostic treatments, the evidence necessary for regulatory approval will be facilitated.

Section 8: Conclusions / Way Forward

The use of advanced radiotherapy techniques, and treatment of cancer patients with radiopharmaceutical therapies, has been incorporated into clinical practice guidelines and received regulatory approvals for a broad range of cancers.However, there are many initiatives that are required to ensure patients have equitable access and availability of these therapies at a global level. We recommend a series of actions to increase access to imaging, diagnostic and therapeutic radiopharmaceuticals and radiotherapy, as follows.

Action 1. Improvement in provision of infrastructure for delivery of advanced radiotherapy, and radiopharmaceutical therapy is required, particularly in LMICs. Addressing the maintenance needs is critical to ensuring the efficiency of diagnostic imaging and radiotherapy treatment in LMICs.

Action 2. Workforce issues require innovative strategies for training and credentialling to enable effective delivery of quality patient care in theranostics and radiotherapy. Development of training programs between countries and not-for-profit entities may assist in improving workforce training. This is particularly relevant for medical physicists, but also for a range of health professionals involved in the delivery of radiotherapy, and treatment of patients with theranostics.

Action 3. Global availability of radioisotopes for theranostics and supply chain reliability are key factors in ensuring equitable access to theranostics, particularly in LMICs.

Action 4. Support of clinical trials for theranostics and radiotherapy techniques will help define best clinical uses and facilitate implementation. Implementing harmonized data standards and embracing digital transformation in radiation medicine are pivotal for advancing research, improving clinical outcomes, and optimizing global cancer care.

Action 5. Support of the regulatory infrastructure in countries to facilitate adoption of theranostics is necessary to ensure safe and effective delivery of radiopharmaceutical therapy to patients.

Action 6. Innovative financial solutions and reimbursement approaches are needed to increase access to radiotherapy and theranostics, and could include a global fund for equipment and infrastructure and workforce development, as well as mechanisms for cost-effective radiopharmaceutical access. Coverage of radiotherapy and theranostics in Universal Health Coverage should be implemented to avoid financial toxicity of patients and increase access.

Action 7. Collaboration and coordination between countries and health care providers involved in this cancer control area is essential to avoid waste and overlap. Political support through country level actions and global consensus building through high level meetings for non-communicable diseases (NCDs) is important as a vehicle for acceleration of progress.

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Table 1.1. Global theranostics utilisation

Index / Therapeutic area	Thyroid cancer & hyper-thyroidism (^{131}I)	Thyroid cancer (^{131}I)	Hyper-thyroidism (^{131}I)	Bone cancer (all)	Bone mets - ^{153}Sm	Bone mets- ^{89}Sr	Bone mets- ^{223}Ra	Bone mets- ^{32}P	Radio-synovectomy (all)
Global utilisation per million population	78.6	35.3	43.2	7.5	0.2	1.6	5.5	0.2	10.5
High-income countries									
Utilisation per million population (range)	161.9 (0.0-61,000)	80.1 (0.0-35,200)	81.8 (0.0-25,800)	37.5 (0.0-33,600)	0.5 (0.0-300)	0.3 (0.0-300)	36.7 (0.0-33,000)	0.0 (0.0-20)	69.6 (0.0-70,000)
Mean (SD)	5,703 (11,687)	2,821 (6,493)	2,882 (5,802)	1,322 (6,137)	17 (57)	12 (55)	1,292 (6,030)	1 (4)	2,451 (12,763)
Median (IQR)	1,148.5 (411.8-7,238.5)	654.5 (225.3-2,965.3)	375.0 (151.5-2,864.8)	14.5 (0.0-112.5)	0.0 (0.0-4.0)	0.0 (0.0-0.0)	4.0 (0.0-97.5)	0.0 (0.0-0.0)	2.5 (0.0-41.8)
Upper-middle-income countries									
Utilisation per million population (range)	125.0 (0.0-229,895)	48.2 (0.0-84,235)	76.8 (0.0-145,660)	5.3 (0.0-11,489)	0.0 (0.0-50)	4.8 (0.0-10,706)	0.1 (0.0-50.0)	0.4 (0.0-783)	0.1 (0.0-100)
Mean (SD)	12,116 (47,633)	4,672 (17,419)	7,444 (30,246)	510 (2,393)	4 (11)	466 (2,232)	6 (13)	36 (167)	8 (23)
Median (IQR)	618.0 (191.0-2,875.5)	348.0 (65.0-1,656.5)	200.0 (45.0-1,069)	0.0 (0.0-7.5)	0.0 (0.0-0.5)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Lower-middle-income countries									
Utilisation per million population (range)	31.3 (0.0-31,906)	17.1 (0.0-20,000)	14.2 (0.0-23,898)	0.5 (0.0-754)	0.3 (0.0-375)	0.1 (0.0-187)	0.0 (0.0-1.0)	0.1 (0.0-215)	0.2 (0.0-300)
Mean (SD)	3,306.2 (7,263.7)	1,804.2 (4,302.6)	1,550.5 (4,451.0)	54.5 (158.4)	34.0 (93.2)	12.7 (43.2)	0.0 (0.2)	7.8 (38.1)	18.3 (70.5)
Median (IQR)	330.0 (30.0-1,945.0)	150.0 (10.0-1,204)	100.0 (20.0-500.0)	0.0 (0.0-2.8)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Low-income countries									
Utilisation per million population (range)	0.3 (0.0-30.0)	0.1 (0.0-20.0)	0.2 (0.0-20.0)	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0)
Mean (SD)	15.8 (12.4)	6.7 (7.5)	9.2 (6.6)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Median (IQR)	15.0 (7.5-26.3)	5.0 (1.3-8.8)	10.0 (6.3-10.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)

Table 1.2. Global theranostics utilisation

Index / Therapeutic area	Neuro-endocrine cancer (all)	Neuro-endocrine (^{131}I MIBG)	Neuro-endocrine (^{177}Lu-DOTA)	Prostate cancer (all)	Prostate cancer- ^{177}Lu-PSMA	Prostate cancer- ^{225}Ac-PSMA	Liver cancer (all)	Liver- ^{90}Y-microspheres	Liver- ^{188}Re-lipiodol
Global utilisation per million population	3.3	0.2	3.1	2.9	2.7	0.1	2.2	2.2	0.0
High-income countries									
Utilisation per million population (range)	17.3 (0.0-8,725)	1.0 (0.0-350)	16.3 (0.0-8,375)	14.5 (0.0-6,250)	14.2 (0.0-500)	0.3 (0.0-250)	13.2 (0.0-10,000)	13.2 (0.0-10.000)	0.0 (0.0)
Mean (SD)	609 (1,634)	36 (75)	573 (1,569)	512 (1,299)	500 (1,254)	12 (48)	466 (1,815)	466 (1,815)	0.0 (0.0)
Median (IQR)	134.0 (10.3-302.8)	3.0 (0.0-29.0)	113.0 (7.8-275.0)	24.5 (0.0-241)	24.5 (0.0-240)	0.0 (0.0-0.0)	20.5 (0.0-246)	20.5 (0.0-246)	0.0 (0.0-0.0)
Upper-middle-income countries									
Utilisation per million population (range)	1.4 (0.0-2,530)	0.1 (0.0-72.0)	1.2 (0.0-2,500)	1.7 (0.0-3,300)	1.5 (0.0-3,000)	0.2 (0.0-300)	0.5 (0.0-1,000)	0.5 (0.0-1,000)	0.0 (0.0-0.0)
Mean (SD)	131 (524)	12 (18)	120 (519)	169 (686)	146 (623)	22 (72)	46 (208)	46 (208)	0.0 (0.0)
Median (IQR)	11.0 (0.0-50.0)	0.0 (0.0-23.0)	0.0 (0.0-25.5)	0.0 (0.0-34.5)	0.0 (0.0-34.5)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Lower-middle-income countries									
Utilisation per million population (range)	0.7 (0.0-2,040)	0.1 (0.0-110)	0.6 (0.0-2,000)	0.6 (0.0-2,000)	0.3 (0.0-700)	0.0 (0.0-60.0)	0.1 (0.0-160)	0.1 (0.0-100)	0.0 (0.0-60.0)
Mean (SD)	71.3 (360.0)	5.6 (20.8)	65.9 (353.2)	65.9 (353.2)	28.6 (124.4)	2.2 (10.7)	8.6 (30.4)	6.7 (21.2)	1.9 (10.8)
Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Low-income countries									
Utilisation per million population (range)	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)

Table 2. Demographics of countries: hypofractionation vs conventional radiotherapy analysis

Income Level	**Total**	**LI**	**LMI**	**UMI**	**HI**
Index	N (%)	N (%)	N (%)	N (%)	N (%)
Countries	174 (100.0)	27 (15.5)	47 (27.0)	45 (25.9)	55 (31.6)
Population (2024)*	8.11 (100.0)	0.75 (9.2)	3.51 (43.2)	2.56 (31.6)	1.29 (15.9)
GDP/capita (average)	15,396	909	2,913	10,224	47,539
RT centres	8,317 (100.0)	31 (0.4)	1,044 (12.5)	2,341 (28.1)	4,901 (58.9)

GDP=gross domestic product; HI=high income; LI=low income; LMI=lower middle income; N=number; RT=radiotherapy; UMI=upper middle income.

* *Population number is presented in billion people.*

Table 3. Incidence and required radiotherapy for prostate and breast cancer

Income level	Total	LI	LMI	UMI	HI
Prostate cancer					
Annual prostate cancer incident (2024)	1,543,533	35,898	172,739	459,057	875,839
Share of incident cases (2024)	100%	2%	11%	30%	57%
Radiotherapy utilisation (58%*)	895,249	20,821	100,188	266,253	507,987
Fractions needed, if CRT (37/course)	33,124,214	770,371	3,706,973	9,851,355	18,795,515
Fractions needed, if HRT (20/course)	17,904,981	416,417	2,003,769	5,325,057	10,159,738
Differences in number of fractions needed, if HRT substitutes CRT	15,219,233	353,954	1,703,204	4,526,298	8,635,777
Additional patients treated with same number of fractions used in CRT, if substituted by HRT	760,962	17,698	85,160	226,315	431,789
Breast cancer					
Annual breast cancer incident (2024)	2,416,075	82,271	580,863	763,746	989,195
Share of incident cases (2024)	100%	3%	24%	32%	41%
Radiotherapy utilisation (87%*)	2,101,986	71,576	505,351	664,459	860,600
Fractions needed, if CRT (25/course)	52,549,640	1,789,390	12,633,771	16,611,481	21,514,998
Fractions needed, if HRT (15/course)	31,134,829	1,073,634	7,580,262	9,966,888	12,514,044
Differences in number of fractions needed, if HRT substitutes CRT	21,019,856	715,756	5,053,508	6,644,592	8,605,999
Additional patients treated with same number of fractions used in CRT, if substituted by HRT	1,401,324	47,717	336,901	442,973	573,733

CRT=conventional radiotherapy; HI=high income; HRT=hypofractionated radiotherapy; LI=low income; LMI=lower middle income; N=number; RT=radiotherapy; UMI=upper middle income.

* *Optimal radiotherapy utilisation, as reported in the Lancet Oncology Commission report "Expanding global access to radiotherapy" (2).*

Table 4. Cost-savings associated with the adoption of HRT compared to CRT in prostate and breast cancer

	Prostate cancer					Breast cancer					Both cancers
Index (USD)/Income Level	**LI**	**LMI**	**UMI**	**HI**	**Total**	**LI**	**LMI**	**UMI**	**HI**	**Total**	**Total [a]**
Annual cost-saving, if HRT substitutes CRT											
Total (million USD) [b]	21.2	110.7	389.2	2,029	2,550	42.9	328.5	571.4	2,022.4	2,956	5,515
Equipment costs	17.0	83.0	214.0	608.8	923	34.3	246.4	314.2	606.7	1,202	2,125
Building costs	2.1	5.5	19.5	101.5	128.6	4.3	16.4	28.6	101.1	150.4	279.0
Salary costs	2.1	22.1	155.7	1,319.1	1,499.0	4.3	65.7	228.5	1,314.6	1,613.1	3,112.2
Annual cost-saving per average GDP/Capita											
Total (million USD)	23,363	38,005	38,073	42,689	165,665 [c]	47,245	112,763	55,892	42,542	192,597 [c]	358,262
Annual cost-saving per average GDP/Capita, per billion population											
Total (million USD)	31,147	10,839	14,849	33,063	20,423 [d]	62,984	32,160	21,798	32,949	23,743 [d]	44,166

CRT=conventional radiotherapy; GDP=gross domestic product; HI=high income; HRT=hypofractionated radiotherapy; LI=low income; LMI=lower middle income; UMI=upper middle income.

a. *Total number refer to the combined figures for breast and prostate cancer.*

b. *Equipment costs constitute 30%, 55%, 75%, and 80% of total costs in HI, UMI, LMI, and LI countries, respectively. Salary costs account for 65%, 40%, 20%, and 10% of total costs in HI, UMI, LMI, and LI countries, respectively. Building costs represent 5% of total costs in HI, UMI, and LMI countries, and 10% in LI countries (2).*

c. *Total annual cost-savings were divided by the weighted average GDP per capita across all income levels ($15,396).*

d. *Total annual cost savings were divided by the weighted average GDP per capita across all income levels ($15,396) and the total population of the sample (8.1 billion).*

Table 5. Eligible patient population for ^{177}Lu-PSMA therapy and number of doses required per year

Index	Eligible patients for ^{177}Lu-PSMA therapy	^{177}Lu-PSMA doses required
Total (globally)	158,162	553,569
Total per million inhabitants (globally)	19.7	68.8
High-income countries		
Total per million inhabitants (range)	56.7 (3.4-20,404)	198.4 (11.7-71,415)
Mean (SD)	1,334 (3,116)	4,668 (10,907)
Median (IQR)	378.6 (41.3-853.1)	1,325.2 (144.7-2,985.9)
Upper-middle-income countries		
Total per million inhabitants (range)	24.6 (2.1-16,630)	86.0 (7.2-58,205)
Mean (SD)	1,399 (3,403)	4,898 (11,912)
Median (IQR)	200.7 (45.1-917.7)	702.4 (157.9-3,211.8)
Lower-middle-income countries		
Total per million inhabitants (range)	5.5 (0.5-4,209)	19.4 (1.9-14,730)
Mean (SD)	399.3 (718.6)	1,397.6 (2,515.1)
Median (IQR)	131.0 (24.8-456.2)	458.5 (86.7-1,596.6)
Low-income countries		
Total per million inhabitants (range)	3.5 (2.8-275.9)	12.2 (9.8-965.8)
Mean (SD)	84.0 (72.6)	293.9 (254.2)
SD		
Median (IQR)	57.4 (35.0-122.2)	200.8 (122.5-427.7)

Abbreviation: IQR= interquartile range; PSMA= Prostate-specific membrane antigen; SD=standard deviation;

Table 6. Key research priorities for LMICs and areas of digital sciences in radiotherapy and theranostics

	Digital sciences
Increase clinical research trials for common cancer types in LMIC; this will require increasing capacity for conduct of clinical trials and collaboration between HIC and LMIC as well as between LMIC	➢ Research infrastructures based on collaborations between academic sites and industry in HIC and LMIC ➢ Capacity development around education of workforce, clinical trial networks, patient groups
Scale-up quality improvement and implementation research in cancer control	➢ Electronic health records for personalized treatment guidelines ➢ Digital image analysis and AI support for treatment planning and response assessment
Develop clinical practice guidelines based on clinical trial evidence from LMIC	➢ Utilise clinical and imaging data from trials in LMIC to confirm role of radiotherapy and theranostics in cancer care, and integrate into clinical practice guidelines

Panel 1.

Radiotherapy Facility Downtime

The effects that challenging LMIC environmental factors have on LINAC downtime and failure modes presents a critical barrier in determining design features to improve the performance of current LINAC technology. An initial LINAC-based study looking at barriers to providing RT services by facilities in Gaborone, Botswana and Nigeria compared to Oxford, UK was conducted in 2018 in which the equipment maintenance logs of LINACs in single locations in Botswana and the UK and multiple locations in Nigeria were reviewed to determine the key factors in downtime.[13] Comprehensive information on equipment failures, downtime, maintenance and service shortcomings was subsequently carried out in 28 African countries.[14]

These data showed that the RT system components causing downtime, listed by importance, include the electron gun, the vacuum pump, the MLCs, the RF source and the software. From the infrastructure (environmental) aspect, power fluctuations are a serious problem in many LMICs .[15] More data were obtained to define the exact dependence of downtime on individual LINAC components or involvement of other aspects of the RT system.[16] Access to spare parts and availability of staff locally that can perform repair or replacement of the part was a significant factor determining the duration of downtime. Figures 4 a,b shows the average downtime in the African Union regions within Africa, and in HIC, based on the survey response. By combining responses by region, a weighted average over many LINACs is provided. As can be seen the Southern Africa number is skewed by South Africa that has many LINACs and has major service centres.

Maintenance and Servicing

Typically the yearly maintenance and service cost of maintaining a radiotherapy machine is around 5-10% of the purchase of the device. Service options can vary depending on what options the hospital has paid for, ranging from a basic service that excludes all repairs of unique parts to a full AI based predictive maintenance model where the failure of many parts are predicted and replaced weeks in advance of their failure. Those taking the latter option achieve a 98% uptime but this is uncommon in LMIC. The survey on maintenance and servicing across 28 countries, undertaken in 2020, covered all linac-based radiotherapy providers in Africa, and selected hospitals in Jordan, US, Canada, Switzerland and UK.[14-16] The study showed a high correlation between GDP and downtime. The study also looked at the ability to fix common faults onsite and spare parts held (Figure 5). The LINAC downtime was significantly higher in sub-Saharan Africa with seven centres with more than 10 weeks downtime per year (80% uptime) with some LMIC centres having almost a full year of downtime, while in high income countries its typically less than 1 week per year (98% uptime). High downtime was also reported in Northern Africa, while in Southern Africa downtime was smaller but still significantly higher than HIC partially due to their relative shorter distance to service hubs. Not all sub-Saharan Africa had similar levels of downtime with two countries reporting low levels of downtime. The study showed that the higher downtime was related to a lack of experienced engineers, a long wait time for spare parts and lack of funding for maintenance engineering. 91% of facilities reported having a service contract . Those using the linac supplier reported significantly less downtime than those using a sub-contractor or local company. Recently there has been a move from linac suppliers to move servicing in Africa in-house as opposed to a licensed third party. Of note is that the survey did not separate licenced and unlicenced service sub-contractors. Of note is that no clear correlation was between the downtime and the value of the service contract was seen. The biggest correlation found was the link between downtime and having spare parts on site, and having staff able to perform maintenance on the RF system on-site. Studies have also shown that preventative maintenance by cleaning the MLC every 6-12 months can significantly reduce MLC faults.[17]

Panel 2.

Stereotactic Body Radiotherapy versus Conventional Radiotherapy for Medically Inoperable Stage I Non-Small Cell Lung Cancer in Mongolia: Low-Middle Income Country Perspective

In Mongolia, lung cancer ranks as the third most diagnosed cancer and the third leading cause of cancer-related deaths in 2020, representing approximately one in every twelve (8.5%) cancer diagnoses and one in every eleven (9.4%) fatalities, with an estimated 485 new cases and 420 deaths.[36] In the past decade, NSCLC management has advanced significantly with improvements in screening, diagnosis, and treatment. Immunotherapy has emerged as a game-changer, enhancing outcomes despite its higher cost.[37] However, access to these innovations remains limited in developing countries like Mongolia, where immunotherapy for NSCLC is not available. Additionally, technical innovations such as Stereotactic Body Radiotherapy (SBRT), which has become the standard for medically inoperable, early-stage NSCLC, face challenges in LMICs due to inadequate infrastructure, despite compelling evidence of its efficacy over conventional radiation therapy.[38] SBRT exhibits higher 2-year survival rates (70% vs. 53%) and better local disease control at three years (87.2% vs. 43%).[38-40]

Research has shown that SBRT is cost-effective compared to conventional radiation in high- and middle-income countries, but this analysis has not been conducted in low middle-income countries (LMICs).[40,41] We assessed the cost-effectiveness of SBRT in Mongolia, an LMIC, from the healthcare system perspective. The Markov model targeted a hypothetical population of 65-year-old men with peripheral, small (<= 3 cm), medically inoperable NSCLC. SBRT was administered at 50–60 Gy in 5 fractions per NCCN 2023 guidelines, while conventional radiation therapy (CRT) was delivered at 60 Gy in 30 fractions. Transition probabilities, costs, and health utility values for the model were derived from local sources and literature. Direct medical and direct non-medical costs, including training and capital costs, were based on values obtained from the public health system.

SBRT, with a cost of $11,169.18, is more cost-effective than CFRT, which costs $13,663.70. Additionally, SBRT demonstrates higher effectiveness with a score of 2.81 compared to CFRT's effectiveness of 1.99. These findings highlight SBRT's superiority in terms of both cost and effectiveness. Given Mongolia's willingness-to-pay (WTP) threshold of $4,274.27, SBRT proves to be a compelling choice for NSCLC treatment in the country. This suggests that allocating resources towards implementing SBRT may offer significant benefits in terms of improved patient outcomes and cost savings within the healthcare system.

Figure 1. Radiotherapy machines per million inhabitants

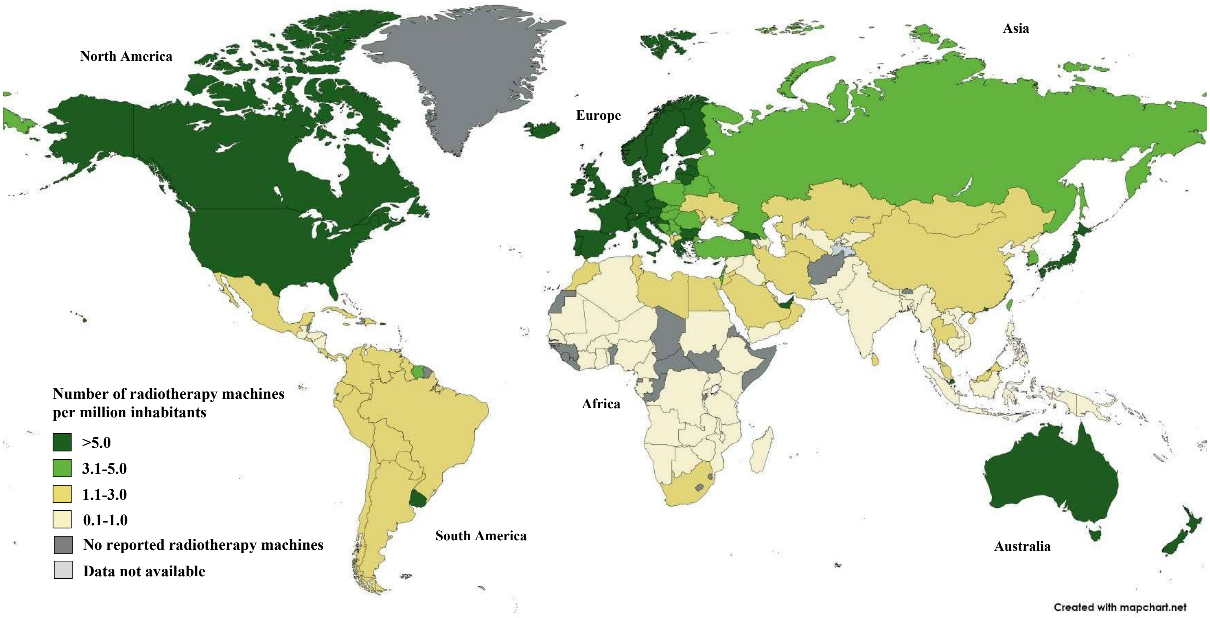
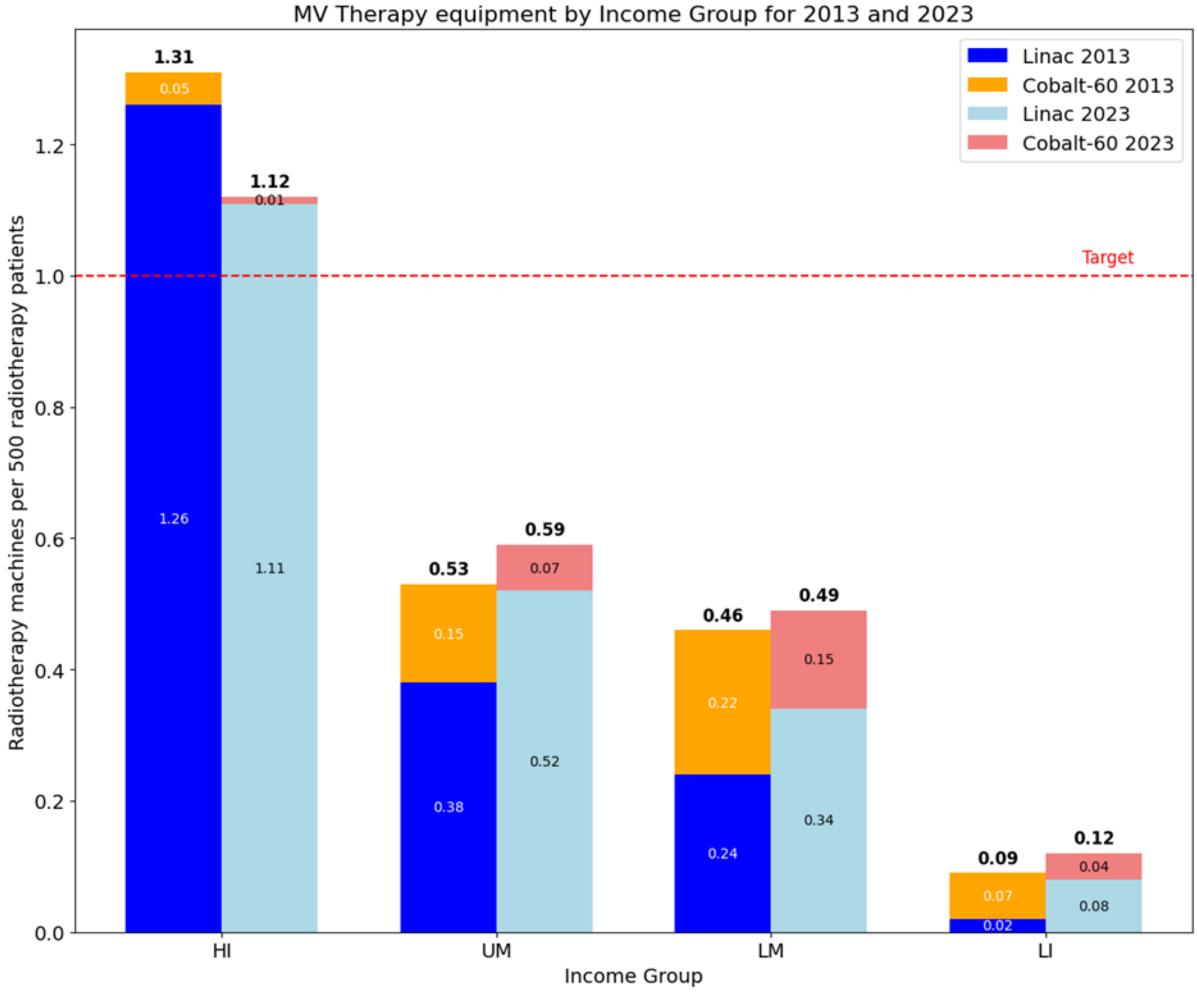


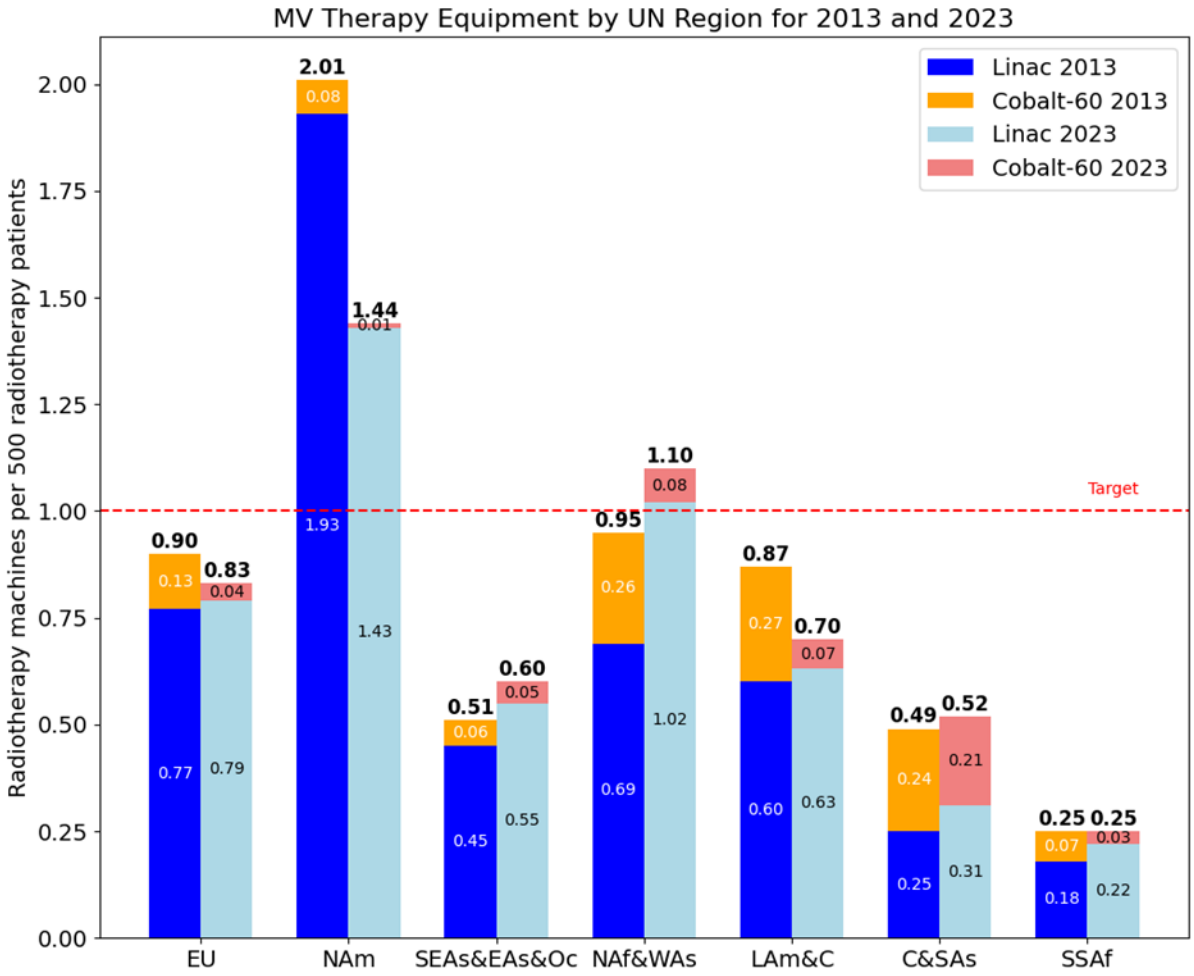
Figure 2. Distribution of high energy external beam radiotherapy machines across country Income Groups in 2013 and 2023.



HI - High Income, UM - Upper Middle Income, LM - Lower Middle Income, LI - Low Income. The target line represents the optimal radiotherapy machine number per 500 patients.

The red dotted line indicates the target of 1 machine for every 500 cases needing radiotherapy per year. This is estimated to be the capacity of one radiotherapy unit per year.

Figure 3. Distribution of high energy external beam radiotherapy machines across UN Regions in 2013 and 2023.



EU - Europe; NAm - Northern America; SEAs&EAs&Oc - South-East Asia, East Asia, and Oceania; NAf&WAs - Northern Africa and Western Asia; LAm&C - Latin America and the Caribbean; C&SAs - Central and Southern Asia; SSAf - Sub-Saharan Africa. The target line represents the optimal radiotherapy machine number per 500 patients.

The red dotted line indicates the target of 1 machine for every 500 cases needing radiotherapy per year. This is estimated to be the capacity of one radiotherapy unit per year.

Figure 4a. Radiotherapy machine downtime in surveyed African countries regions compared to high-income countries.

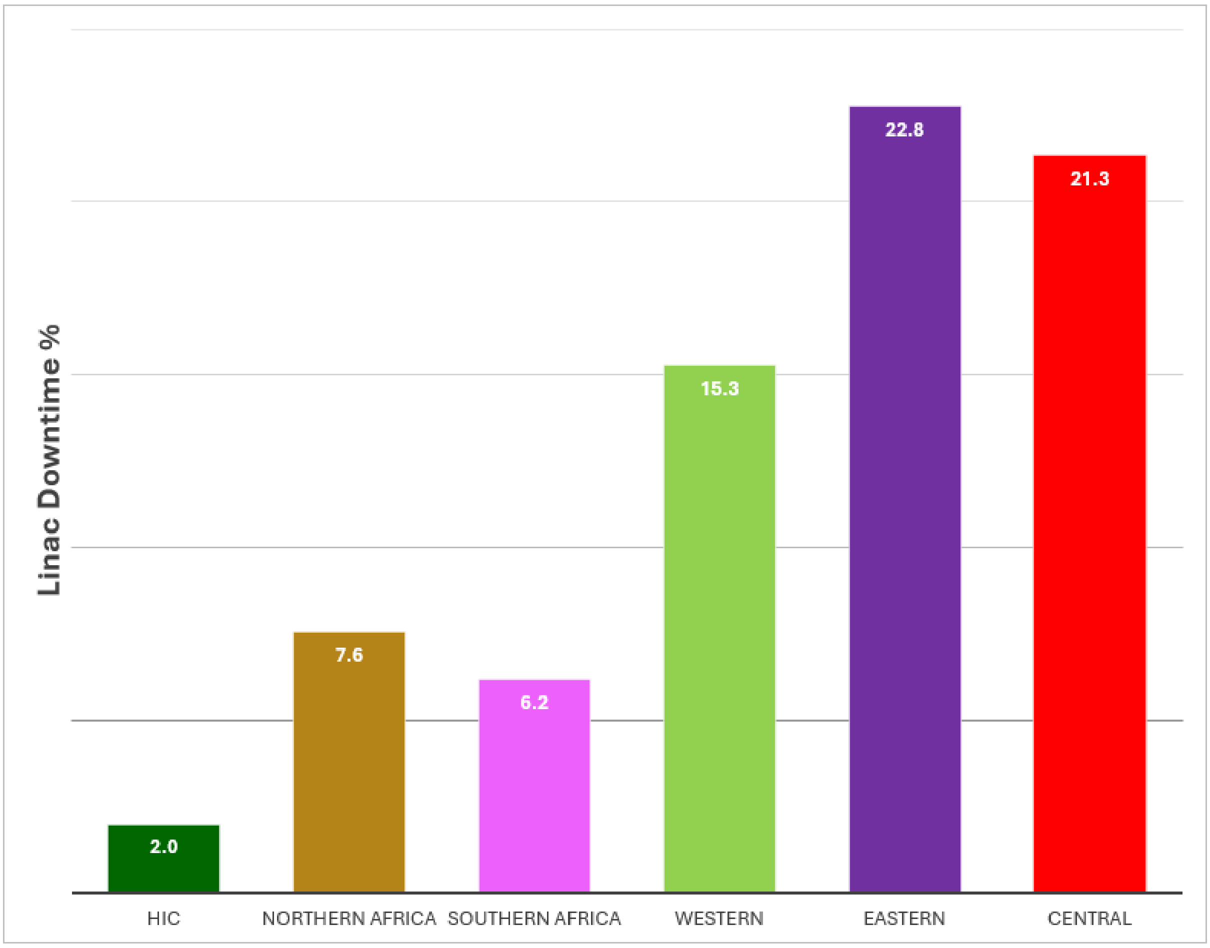


Figure 4b. Reported unscheduled downtime for LINAC-based radiotherapy facilities in Africa.

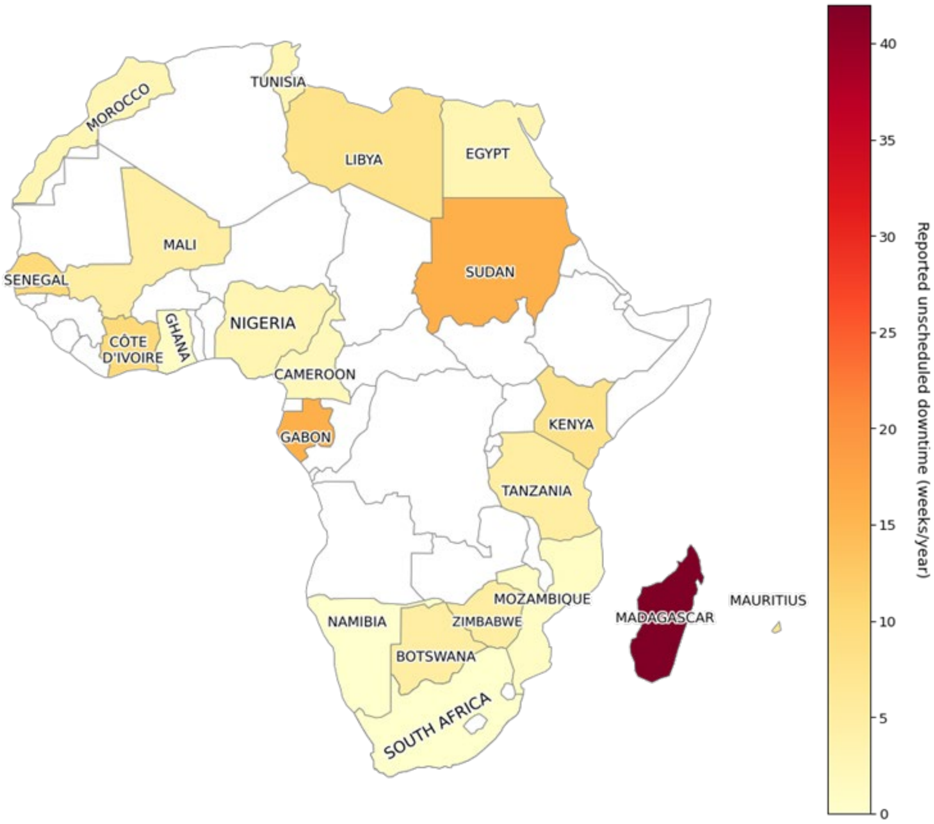
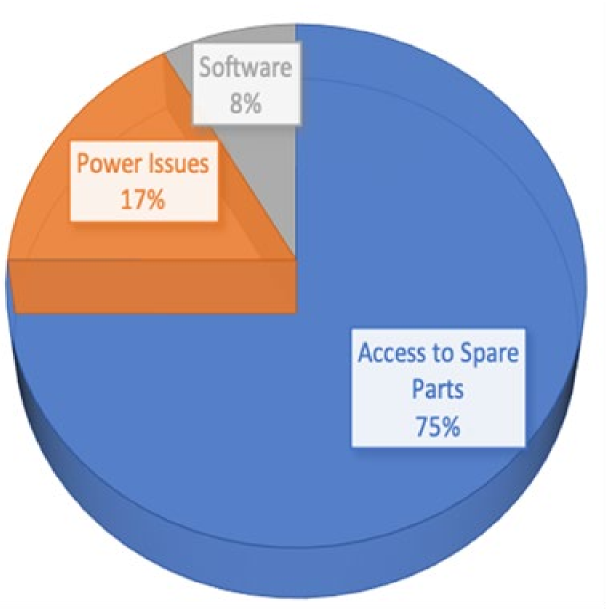
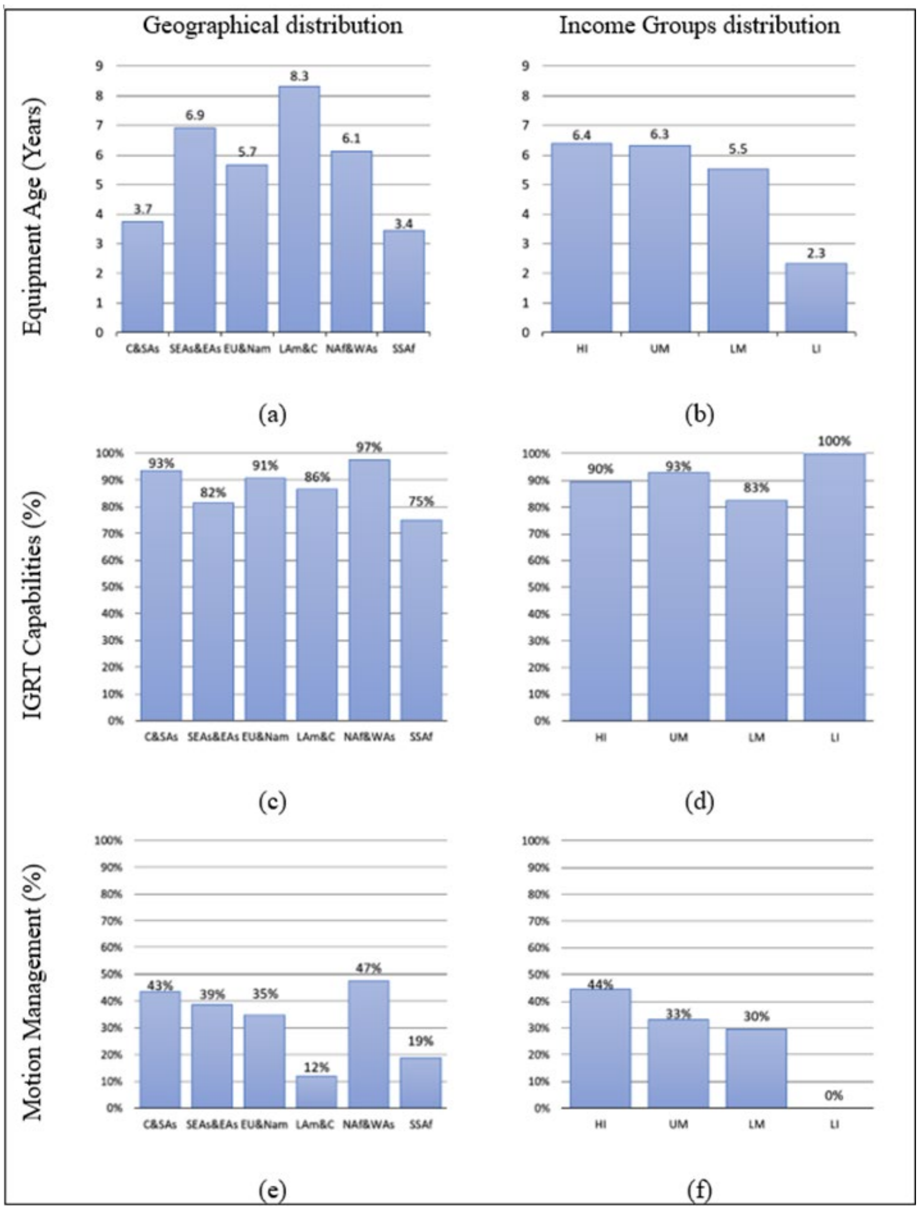


Figure 5. Major reasons for LINAC downtime in 28 countries.



- **69%** do not have access to spare **RF Sources**.
- **67%** do not have access to spare **Vacuum Pumps**.
- **24%** do not have access to spare **MLCs**.
- **47%** do not have access to spare **Electron Guns**.

Figure 6. LINAC IGRT and MM capabilities, and equipment age



(a) equipment age distribution across the UN regions, C&SAs - Central and Southern Asia; SEAs&EAs - Eastern and South-Eastern Asia; EU&NAm - Europe and Northern America; LAm&C - Latin America and the Caribbean; NAf&WAs - Northern Africa and Western Asia; SSAf - Sub-Saharan Africa, (b) equipment age distribution across the county income groups HI - High income, UM - Upper middle income, LM - Lower middle income, LI - Low income, (c) IGRT capabilities availability distribution across the UN regions, (d) – IGRT capabilities availability distribution across the county income groups, (e) motion management capabilities distribution across the UN regions, (f) motion management capabilities distribution across the county income groups.

Figure 7. Use of ^{131}I in hyperthyroidism and thyroid cancer

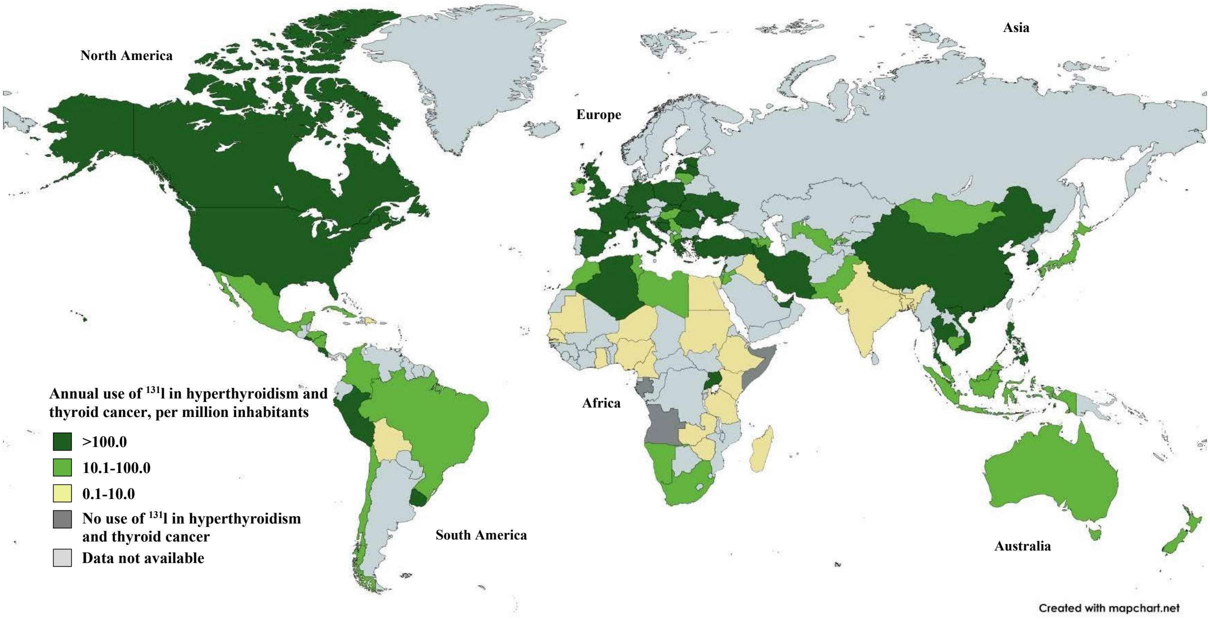


Figure 8. Use of radiopharmaceutical therapy in bone cancer

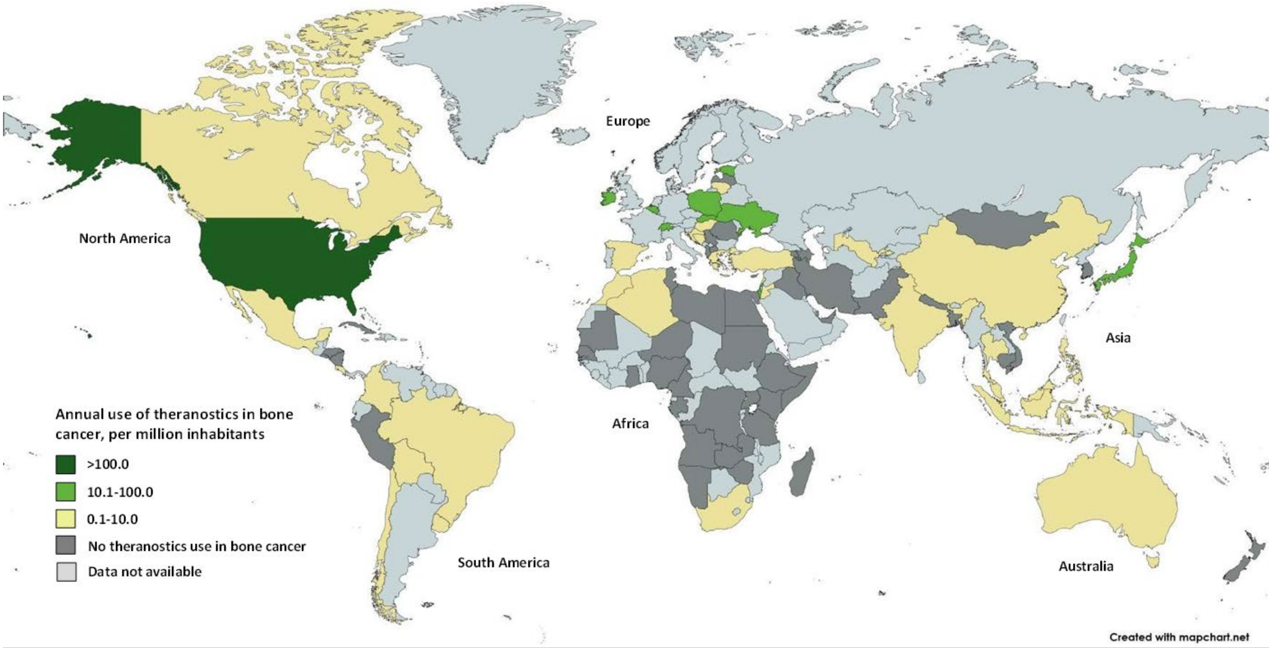


Figure 9. Use of ^{131}I-MIBG and ^{177}Lu-DOTATATE in neuroendocrine cancer

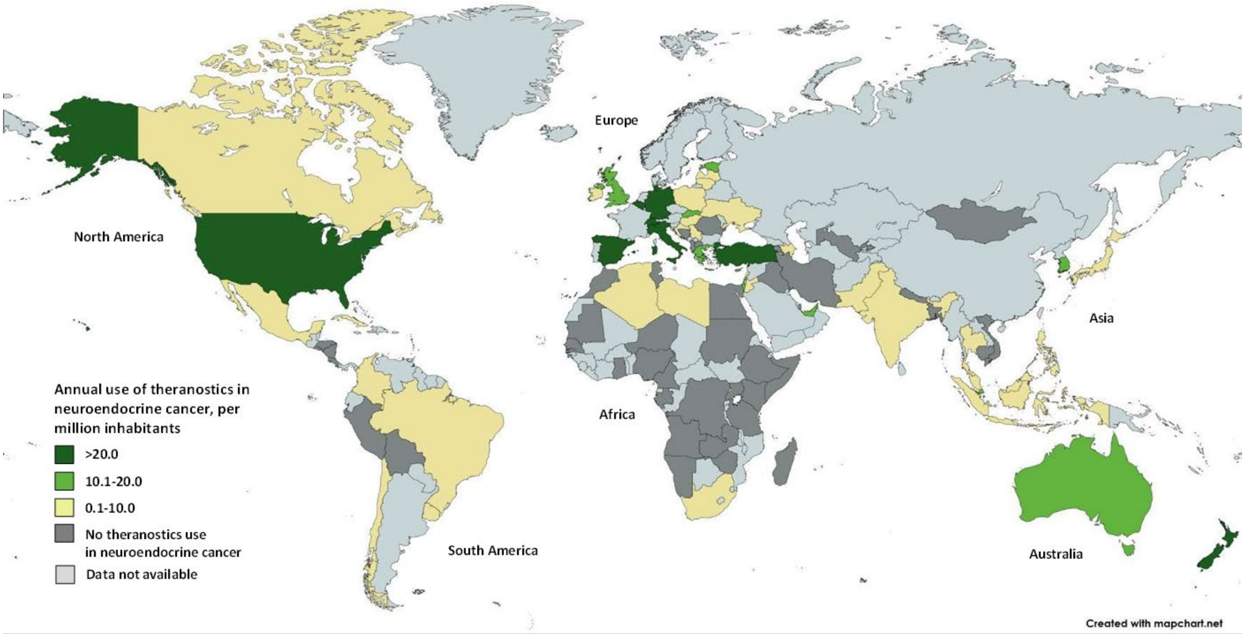


Figure 10. Use of ^{177}Lu-PSMA and ^{225}Ac-PSMA in prostate cancer

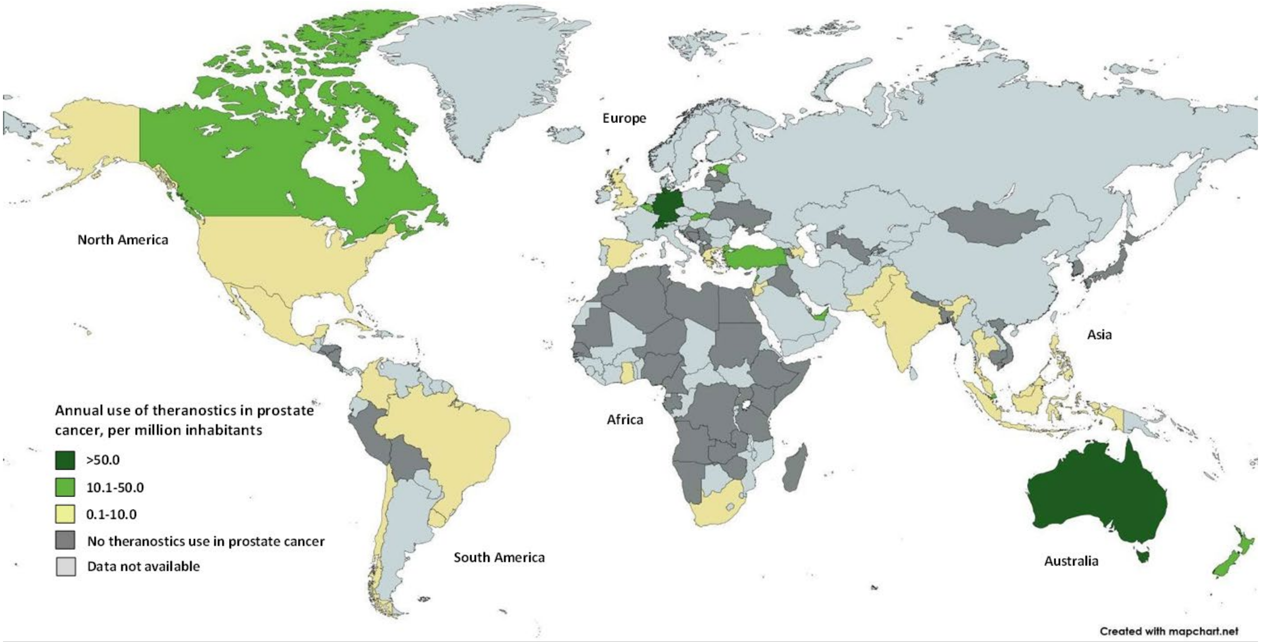
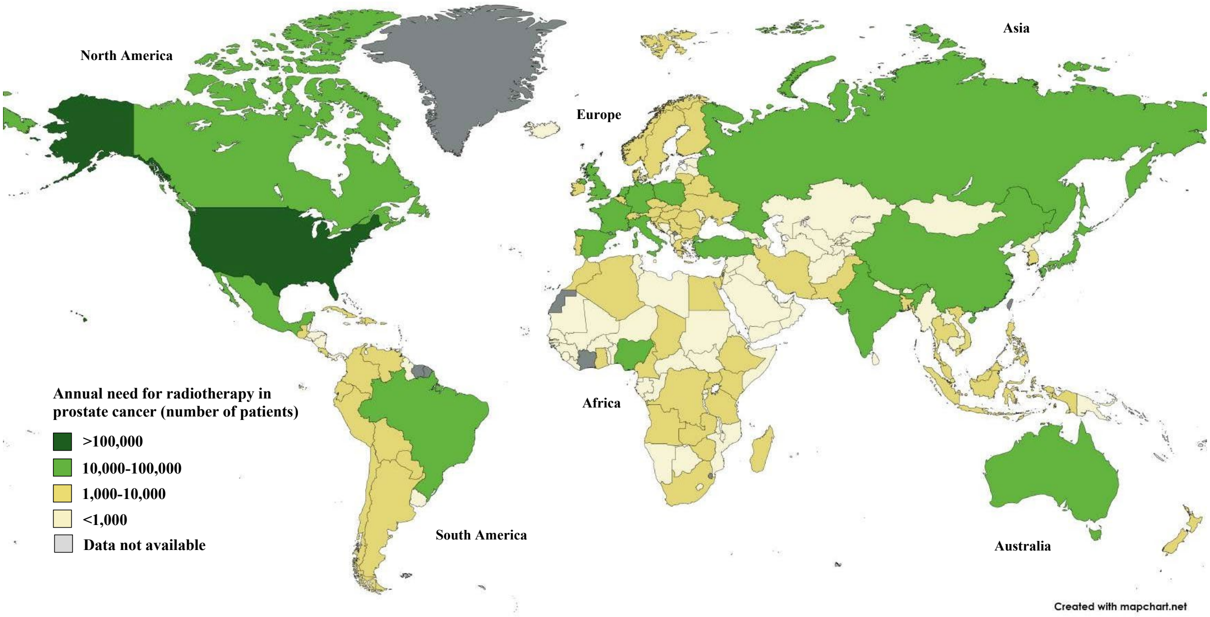


Figure 11. Calculated annual global need for radiotherapy in prostate and breast cancer

a. **Prostate cancer**



b. **Breast cancer**

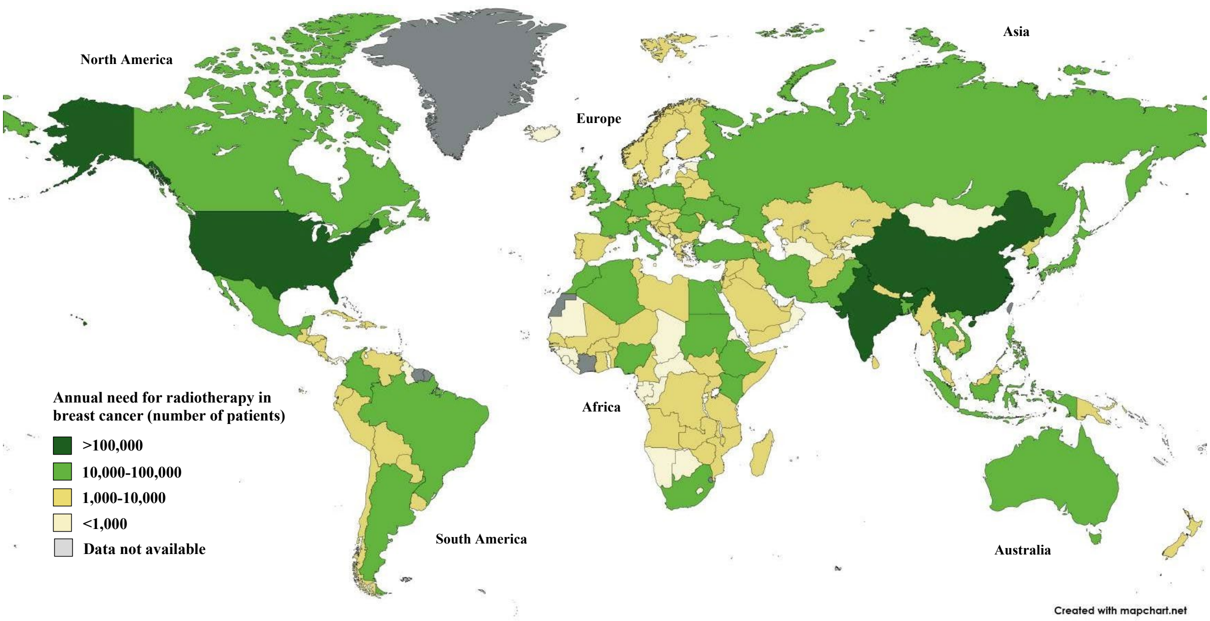
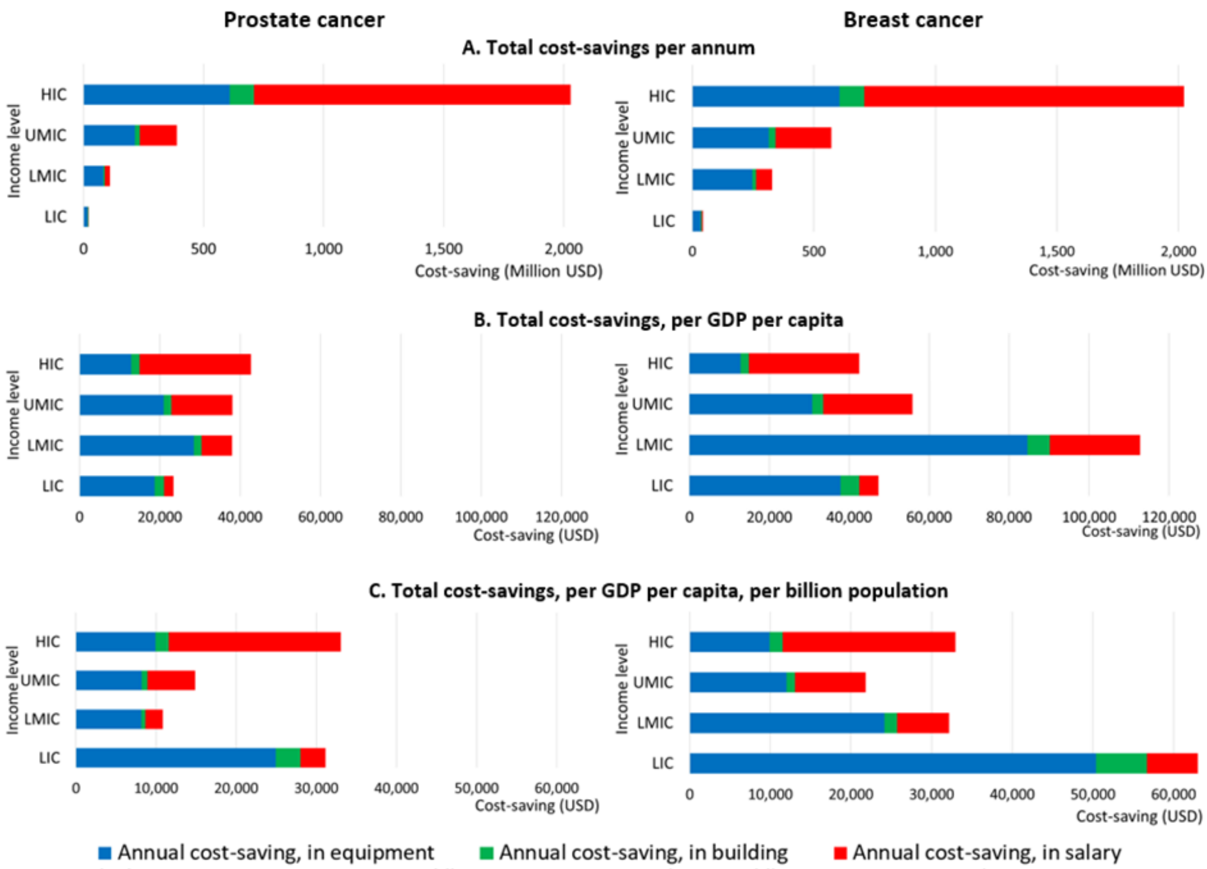


Figure 12. Cost savings associated with the adoption of HRT versus CRT



HIC=high income country; UMI=upper middle income country; LMI=lower middle income country; LIC=low income country

Figure 13. Global patients eligible for ^{177}Lu-PSMA therapy

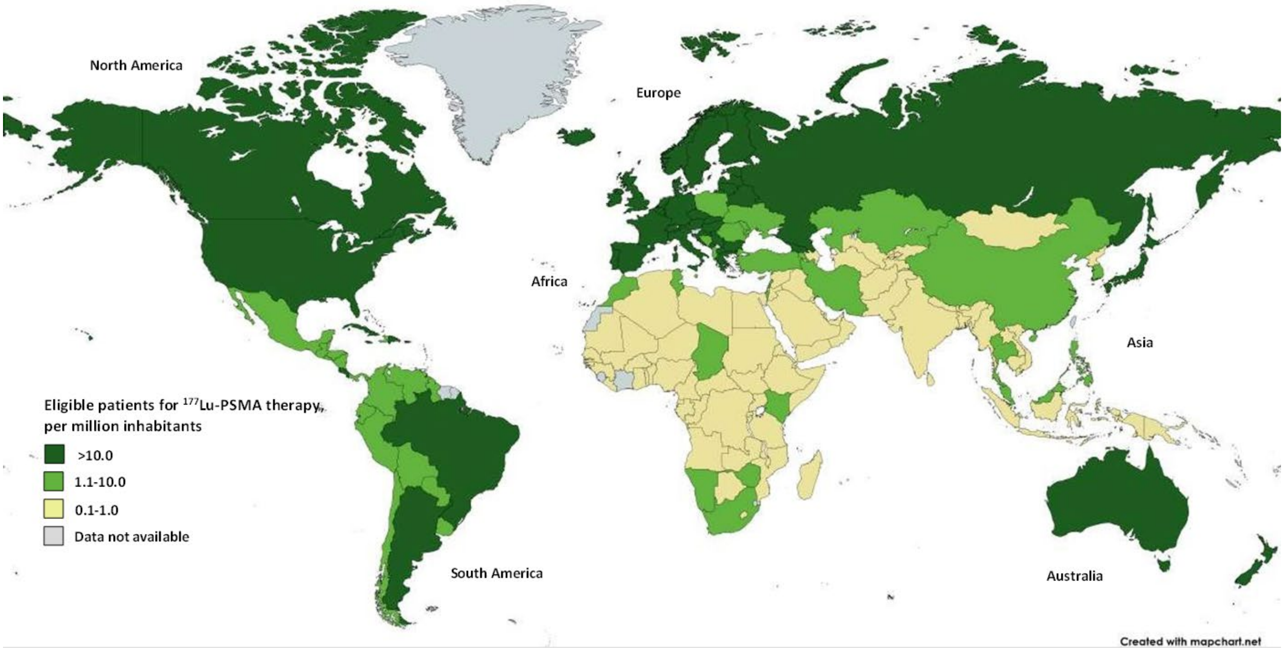


Figure 14. Ratio ^{177}Lu-PSMA cost per treatment/GDP per capita in 2024

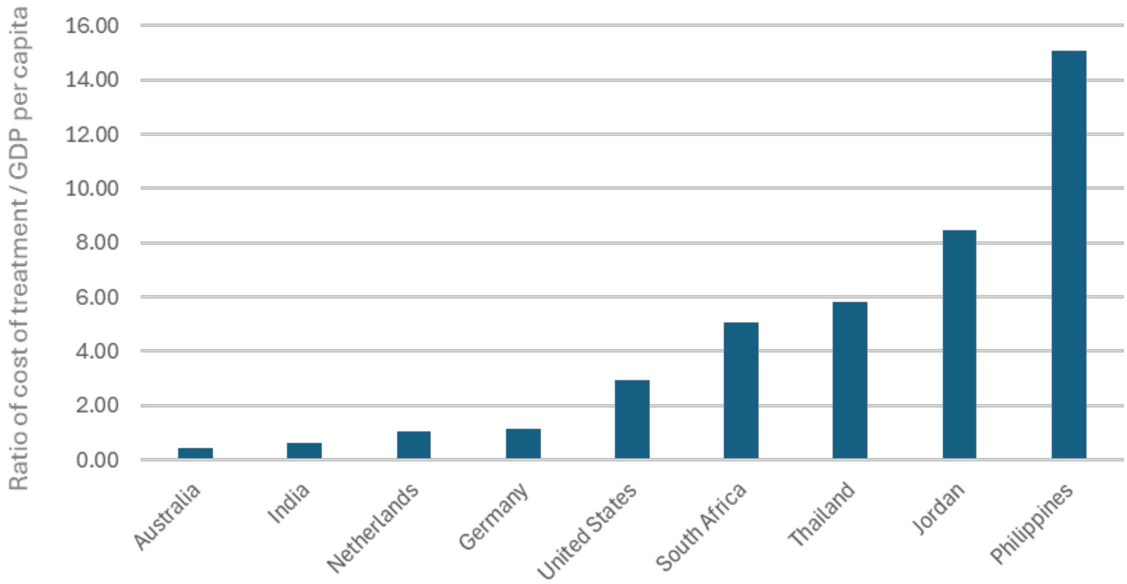
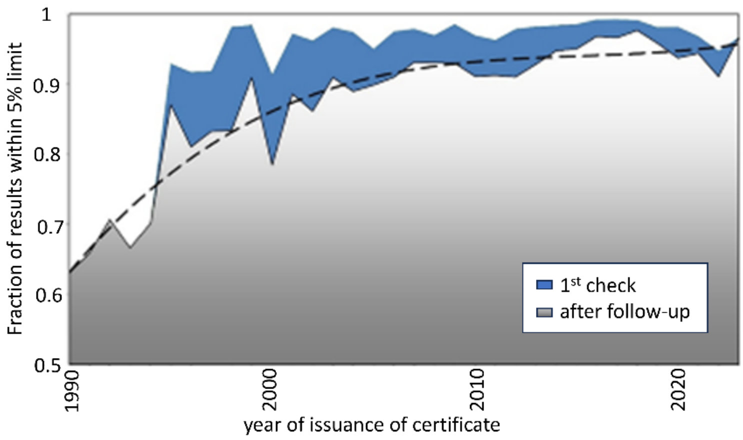


Figure 15. Dosimetry audit results.



Fraction of the dosimetry audit results within the 5% acceptance limit for radiotherapy hospitals during the period 1990 – 2023. The grey area indicates the results obtained in the first check, and the blue area corresponds to the percentage of those after a subsequent follow-up.

Figure 16. Inclusion of radiotherapeutic-care services for breast, cervical and lung cancers in countries' largest public-sector Health Benefit Packages, by WHO region and World Bank income group