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Is the fast-paced technological advancement in radiation treatment equipment good for Indian Scenario? No☆

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ABSTRACT

Around 60% of new cancer patients and 23% of previously radiotherapy-treated patients need radiotherapy for management of their cancer. Although radiotherapy demands <6% of budget of cancer, huge initial out-lay makes it apparently expensive. Technological innovation has increased number of radiotherapy planning and delivery equipments at an unprecedented rate. Improved precision of technological innovation has decreased the clinical adverse events albeit the questionable accuracy of dose delivered. However, new radiotherapy equipments are expensive, sophisticated and difficult to operate without any difference in survival. Novel technology has decreased access to radiotherapy in resource-constrained developing countries. Tele-therapy and brachytherapy machine with Co-60 radio-isotope as the source of radiation may be feasible and inexpensive option for countries like India. Advanced techniques and linac-based therapy may be restricted for selective cases and should always be carried-out within the scope of clinical trials.

India is seventh largest country in the world by area and second most populous country with 1.24 billion people. Indian nominal and purchasing power parity (PPP) gross domestic product (GDP) is tenth and third largest in the world respectively. India has emerged as one of the fastest-growing economies in the world [1]. All of booming Indian economy, significant contribution of the new industries to the robust economy, willingness to gradually become independent of foreign aid, abundant natural resources, well-established indigenous manufacturing industrial sector, capability to manufacture nuclear power and weapons, and world-envying highly sophisticated and modernized space programme has helped India to make its appearance in various world leaders' summit. Due to its increasing global influence, India is in race for the permanent membership of World Security Council. India has been visualized as a future new engine of World Economy [2–6]. With this background, it would not be inappropriate, irrelevant for India to aspire to have and treat patients with state-of-art, advanced, latest, up-to-date armamentarium of radiotherapy equipments. The field of radiation oncology has witnessed unprecedented technical advances after 1980s that included new imaging modalities (4-D computed tomography, functional magnetic resonance imaging and molecular imaging) to simulate the patients for more accurate delineation of tumour and critical normal tissues, robust radiotherapy planning computers and software (algorithm) for smart-segmentation, auto-contouring, radiation beam optimization and dosimetry and precise target localization (continuous image guidance of cone-beam computed tomography and fluoroscopy, gating of beam to track the moving targets, phenomenal control of movement of couch and direction by robotics) and novel implementation systems such as advanced linear accelerators [7].

Discovery of X-ray and radium by Wilhelm Codrad Roentgen and Marie Curie in years 1895 and 1898 respectively marked the beginning of treatment of cancer with radiation therapy. Radium-226 (Ra-226) was the radioisotope used to treat cancer by both teletherapy and brachytherapy until it was replaced by Cobalt-60 (Co60) in 1951 due to concern of long half-life of Ra-226. Around the same time, medical linear accelerators emerged as an alternative source of mega-voltage radiation. Much advance in the planning and delivery of radiotherapy is possible with the advent of three dimensional imaging, differentially moving 5 cm thick lead leaves of multi-leaf collimator (MLC), application of computers. Coutard's

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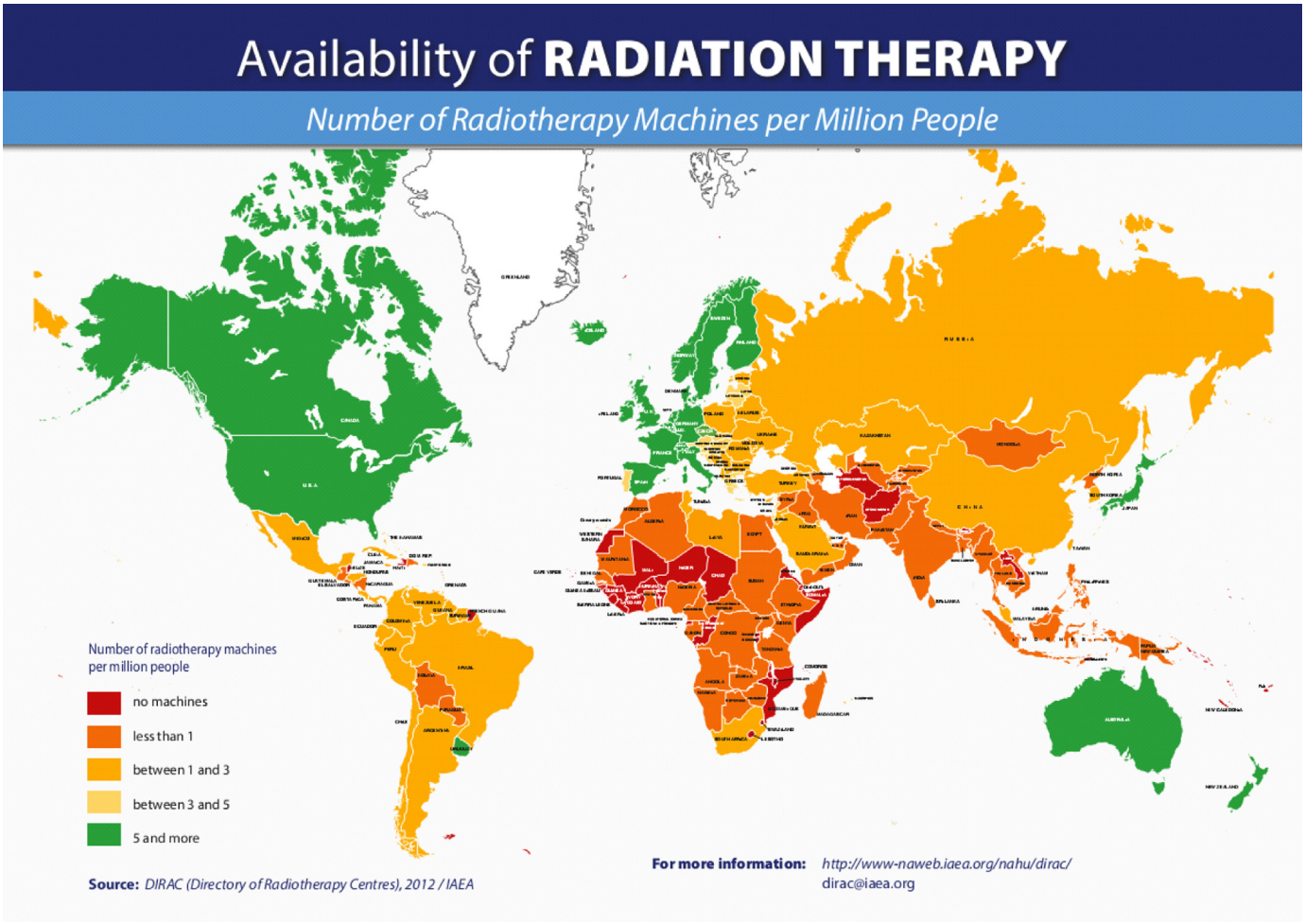

Fig. 1. Availability of radiotherapy machine per million population around the globe. Directory of Radiotherapy Centres (DIRAC) 2012 of IAEA shades nation across the world according to available number of radiotherapy machines per million population in each of the countries. This map was produced in 2012, using information from the IAEA Directory of Radiotherapy Centres database [3].

Permission for using this map has been obtained from IAEA through the Email IDs: S.Loof@iaea.org & Info@iaea.org on 28th August 2014.

observation of results of animal experiment of Claudius Regaud inspired him to develop fractionated radiotherapy. Conventionally fractionated radiotherapy has been the standard of care since then. Waxing and waning interest on the clinical use of altered fractionation, hypofractioned radiotherapy, stereotactic radiotherapy and radio-surgery is evident right from the beginning of clinical radiotherapy to date [8].

India was and is fortunate to be one of the early beneficiaries of western discovery and invention. India commissioned the first Co60 teletherapy unit at the Cancer Institute, Chennai in 1956. Deep X-ray therapy and radium brachytherapy were used in almost all the cancer facilities across India [9]. Cancer hospitals in India are taking pride of executing the latest of technology in radiotherapy and are on their marks to acquire, expertise and propagate any of the contemporary technology that may be launched in market in the near-future [10]. Given the extremely advantageous position of India among the countries of the world, magnitude of the Indian economy, technical skills and expertise, one would naturally expect gleaming India in the world map of availability of radiotherapy machine per million population released by International Atomic Energy Agency (IAEA).

However, Directory of Radiotherapy Centres (DIRAC) 2012 of IAEA has grouped India (Fig. 1) with poorest Sub-Saharan African countries with less than one radiotherapy machine per million people [11]. Apathetic state of Indian radiotherapy cannot be explained by gigantic population, difficult geography, magnitude of land surface area or the booming economy. Aforementioned reasons do not find validity and basis if we compare ourselves with our immediate neighbour Peoples' Republic of China, another emerging economy with similar socio-economic, demographic, geographic and cultural profile [6]. Current Indian radiotherapy scenario is gloomy reflection of the sad state-of-affairs of both Indian health systems as well as the stagnant human development indices (HDI) [12,13]. India ranks 140th and 136th in the world in nominal GDP per capita and HDI respectively [14]. India is faced with challenges of poverty, illiteracy, corruption, malnutrition, inadequate public healthcare and insurgence [15]. India has largest number of people living below the world bank's poverty line of USS 1.25 per day [16]. Economic inequalities between rich and poor have grown consistently since 1991 [17]. Nearly half of children under the age of 5 years are underweight and malnourished. The prevalence of child undernutrition in India is among the highest in the world, nearly double that of Sub-Saharan Africa [18]. India spends 4.1% of its GDP on health compared to 7.6% and 5.2% of GDP expended by USA and China respectively [19]. Indian nominal GDP per capita has grown at rate much lower than other Asian developing countries and is expected to remain so in the coming years [20]. Various international financial agencies have downgraded credit rating of India in recent years. Although, standard and poor has upgraded credit rating after the election of new government, this upgradation is merely

based on assumption of implemention of policy reforms and not on the performance of Indian economy. The doubt about comprehensive recovery of Indian economy has also been cast by Governor of Reserve Bank of India as late as September 2014. With the prevailing socio-economic situation, we cannot expect drastic increase in health-care funding, especially the funding for radiotherapy units [21].

Each year in India, there are roughly one million new cases of cancer and ~50% of them require radiotherapy [22,23]. Assuming one machine treats 500 new cancer cases, we need a total of 2000 machines at the current incidence rate of cancer. For the year 2014, ICMR has estimated the new cancer cases at 1.2 millions and a total of 2400 external beam radiotherapy machines are needed. India has nearly 1,00,000 cervical cancer patients and brachytherapy forms integral part of therapy of carcinoma cervix [24,25]. Assuming each machine can deliver 3 fractions of high-dose-rate brachytherapy at an interval of 1 week to 5 patients per day, 400 patients of carcinoma cervix are treated per year per machine and we need 250 brachytherapy machines. According to Atomic Energy Regulatory Board, India has 469 teletherapy machines (237 Co60 + 232 medical accelerators), 15 advanced therapy machines (7 Gamma knife units + 1 super gamma system + 3 tomotherapy + 2 cyber-knife + 2 intra-operative radiotherapy) and 275 brachytherapy machines [10]. As per international standards, current Indian requirement of radiotherapy professionals are as follows: 3300 radiation oncologists at the rate of 1/300 patients, 2500 radiation physicists at the rate of 1/400 patients, 3300 treatment planning staff at the rate of 1/300 patients, and 6–7000 radiotherapy technologists at the rate of 3 per machine treating up to 40 patients [26]. Apart from projected present requirement of radiation man-power, Task Force Report for XI plan has also documented shortage of radiation oncologist [27]. There are many instances of Atomic Energy Regulatory Board (AERB) suspending and resuspending the license of radiotherapy departments both in the national capital and periphery of India to operate even the basic radiation therapy machine due to shortage of adequate number of radiotherapy staff, calibrated dosimeters and survey meter for satisfactory performance of Quality and assurance (QA) [28,29]. To bridge the existing gap in infrastructure and resources, National Cancer Control Programme (1975) has aim of establishing oncology wing in all the medical colleges with Rs. 2 crores of financial assistance for procurement of cobalt therapy unit [30]. By committing itself to finance Co-60 teletherapy unit, National Cancer Control Programme has emerged as a relevant programme in Indian context. IAEA too has regarded Co-60 as "friendlier" treatment machines to place in new low-resource departments with regards to cost, the training required, treatment delivery, planning, and maintenance. In contrast, linac treatment is seven times more expensive than the therapy by Co-60 in view of higher installation cost, limited life span of 10–12 years, training of personnel, frequent machine break-down, costly and limited supply of spare parts and maintenance [31]. Cost consideration is also an important factor in determination of treatment choice and quality of life of patients. Technological innovation is associated with conflict of interest due to high initial cost of clinical application of the technology. Investigations have also revealed nexus of health-care professional trusting latest radiotherapy technology on patients solely for the purpose of financial incentives leave apart its rapid adoption in clinics [32]. Many experts committees have gone overboard at alienating Co60 in favour of much more expensive linear accelerators thereby furthering the misery [9]. Only 1% of Indian population have health insurance and just under 7% work in organized sectors. Therefore it is very obvious that India's private expenditure on health accounts for 72 percent of the total health expenditure. Out-of-pocket medical expenditure is 89% of total health expenditure. As a consequence, 39 million people (3.2% of Indian population) are pushed into poverty every year because of health care costs [33]. In our quest to propagating newer technologies, we should not be responsible for bankruptcy of our patients.

Latest health insurance scheme of government of India has significantly reduced the mortality and out-of-pocket expenditure for cancer. It covers range of radiotherapy technology from Co-60 to IMRT. However, we have to bear in mind that funding for such schemes are provided by generous grants of World Bank. And unprecedented unjustified radiotherapy technological application may only increase India's international debt and deficiencies that have to subsequently be repaid along with interest by common citizens of India [34].

QA programme are more complex for linac and need perennial electricity supply unlike Co-60. Other disadvantage of advanced radiation therapy equipments are as follows: Existing QA guidelines are often inadequate for these new technologies. New QA procedures are needed and are under development. Errors in measurement can be substantial and several new treatment machines provide radiation beams that do not comply with the reference field dimensions given in existing dosimetry protocols thereby complicating the accurate determination of dose for small and non-standard beams. IMRT requires increased attention to physics and dosimetry, more equipment, training and technical support, and more time for quality assurance. IMRT and all other advanced radiotherapy techniques demand increased clinician time for target and organ outlining, increased planning time (initially), and increased machine treatment time in addition to extensive QA programme [31,35]. With the prevailing shortage of radiation oncology resources, it is not practical for resource-constrained countries like India to implement and verify the latest treatment technology. Also of concern is unavailability of clinical data currently on long-term outcome of advanced radiotherapy delivery system. Randomized trials to generate outcome data of tumor control, morbidity, mortality and safety of the different novel procedures are yet to be planned for many. Adding to the former, Claims in support of previous statement is established by the fact that late toxicity profile of ablative radiotherapy has never been published till date [36].

After extensive review of radiotherapy situation across the world, more so of low and middle income countries (LMIC), IAEA initiative Advisory Group on Increasing Access to Radiotherapy Technologies in developing countries (AGaRT) engage the manufacturers, users and experts in open forum. AGaRT is recognized as a significant step towards providing a viable solution (affordable, suitable and sustainable radiotherapy equipment) to the global shortfall of radiotherapy units. Aim of AGaRT is to encourage development of US$ 1 million radiotherapy package of safe, high quality, uncomplicated, easy to handle even by inexperienced, simple to control and maintain essential Co60 and linac radiotherapy technology that does not require frequent calibration, dosimetry measurement and onsite presence of medical physicist. Commissioning of radiotherapy machine to life-time maintenance of linac by regional experts developed under the package by the radiotherapy suppliers and subsequent repatriation are all included in this package [37].

Co-60 radiotherapy equipment is in vogue in most of the developing countries possessing at least one radiotherapy machine. Co-60 can effectively and safely irradiate prevailing tumors in these region by time-tested conventional techniques. However, treatment technique with Co-60 or non-MLC linac is not sufficient to treat all the patients especially those with tumours of thorax, abdomen, posterior neck after the tolerance limits of spinal cord and some superficial and acral tumours. Linac or Co-60 based computer-assisted 3-D conformal radiotherapy is all that is needed to treat these tumours. IMRT is increasingly becoming popular now-a-days even in developing countries. Nevertheless, the dose gradient of IMRT in many cases may not be sufficient to spare

normal tissue and can only be marginally better than 3-D conformal radiotherapy. Another important limitation of IMRT is that it may not fulfill all the normal tissue dose constrain and may sometimes dump excess dose into other adjacent or remote critical normal organ. Particle therapy holds promise of significantly avoiding critical adjacent normal tissue by the virtue of Bragg's peak .i.e. most of the energy of particle are release just before they come to rest. Unfortunately, particle therapy is available only in limited centres across the world due to its cost consideration. Linear accelerator generating 6 MV photon beam with additional capacity to deliver single energy electron beam or Co-60 therapy machine capable of highly conformal treatment technique is more than sufficient to treat most of the tumours presenting in undeveloped regions of the world. More sophisticated technology is rarely required as 70% of tumours in developing countries are locally advanced. X-ray simulator, CT simulator, mould room, computer treatment planning system for 3-D CRT and brachytherapy planning are essential and sufficient for radiotherapy planning process. Remote after loading high-dose rate brachytherapy is yet another requirement for comprehensive cancer care facility.

Key messages

a. Co-60 teletherapy equipment with multi-leaf collimators is all that is needed for comprehensive radiotherapeutic management in developing countries including India.
b. Ir-192 (half-life of 73.83 days) is commonly used as radioactive source for brachytherapy. Co-60 (half-life of 5.3 years) can replace Ir-192 as brachytherapy source in developing countries.
c. Resident doctors should be encouraged to participate in all aspects of handling of Co-60 tele-therapy and brachytherapy equipments in order to increase access to radiotherapy. They should be trained for carrying-out and reporting QA & QC of Co-60 machines.
d. Linac with specialized radiotherapy can be housed in referral, tertiary and regional cancer centres. Clinical and physical research of new techniques and technology has to be encouraged for safe, accurate and precise delivery of radiotherapy.
e. Health-care providers in developing countries has to be made accountable for non-functioning of radiotherapy departments.

Conclusion

2/3rd of all cancer patients need life-saving radiotherapy at some point of their illness. Although cheapest modality of anti-cancer therapy, huge initial out-lay for radiotherapy department may make it apparently expensive and unaffordable. Unprecedented technological advances in radiotherapy have failed to increase survival, has raised new questions on accuracy of dose delivered and have further skewed distribution and available of radiotherapy resources in developing countries. MLC equipped Co-60 radiotherapy machine or low-energy linac with capability to delivery electron along with Co-60 radio-isotope based high-dose-rate brachytherapy unit can constitute comprehensive radiation oncology and cancer centre in developing countries. Teletherapy and brachytherapy machine with Co-60 radio-isotope as the source of radiation may be feasible and inexpensive option for community-based centres in countries like India. Linac with specialized radiotherapy can be housed in referral, tertiary and regional cancer centres. Linac-based and non-linac-based advanced techniques may be restricted for selective cases and should always be vigorously evaluated within the scope of clinical trials over long-follow-up period for both tumour control and adverse events outcomes.

While attempting to reply to the discussion forum on the topic "The fast-paced technological advancement in radiation treatment equipment is good for Indian Scenario," we are neither antagonist of nor dis-contended with fast-paced technological advancement in the field of radiation oncology. We believe that we should always be part of such technological advances by continuously contributing to the progress of science and well-being of mankind. Science has always been dynamic irrespective of ages and era and our duty, as scholars, scientists and physicians, is to relieve the suffering of people with the technology that is relevant, appropriate, affordable, socio-culturally acceptable, safe with comparable risk-benefit ratio to the standard of care technology. Medical practitioners have to strike a fine balance between delivering affordable radiotherapy services to community and contributing towards the latest advancement in their area of expertise with tilt under all circumstances favouring the patients to alleviate their misery. From the above discussion, we would like to conclude that the HDI, pattern and presentation of malignant lesions, available resources and budget outlay do not endorse the use of advanced radiotherapy technology in Indian context.

Conflict of interest

The authors have no conflict of interests to disclose.

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