Chapter 6 Proposal for Establishing a New Radiotherapy Facility



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Introduction

Cancer is a significant cause of morbidity and mortality. As per multiple cancer registries, the incidence of cancer is increasing worldwide. The highest increase is observed among low- and middle-income countries [1]. Radiotherapy is a crucial and cost-effective component of cancer care and can be utilized in the definitive, adjuvant, and palliative settings. Radiation therapy has been shown to increase overall survival in many types of locally advanced cancers. Around half of all cancer patients will receive radiation treatment at some point during their course of treatment [2, 3].

A radiotherapy facility is an integral component of a multidisciplinary cancer center. Along with surgical intervention and chemotherapy, radiotherapy is crucial and needed in designing a cancer care facility. Once the decision to establish a radiotherapy facility has been made, careful strategic planning is needed to ensure alignment with the cancer center's overall mission and goals concerning available resources. Recruitment of skilled clinicians and personnel is critical to ensure safe and high-quality patient care. Coordination and monitoring of the planning and timelines are critical to a successful project, especially when resources are limited. The professional team required to design, construct, and commission a radiotherapy facility needs to be in a multidisciplinary sitting from various background [4].

This chapter presents an overview of radiotherapy's value in treating the most common clinically indicated malignancies worldwide. We aim to present a proposal

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to assess the radiotherapy facility's clinical, infrastructure, and resources need while establishing a new radiotherapy facility.

Population Description

Determining the need for radiation therapy requires in-depth knowledge of the population demographics, cancer incidence, and national disease burden estimates with precise projections for the future [5]. Establishing cancer registries is essential for estimating the community's clinical needs, developing clinical pathways, and implementing research programs. Further forecasts regarding anticipated radiotherapy capacity and use (number of radiation courses and fractions per course for each cancer type, as well as the amount of potential retreatment) should also be estimated [6]. These steps are unique for each nation and country. In the countries where these variables are not measured, the International Agency for Research on Cancer (IARC) provides the best estimate of crude incidence, Table 6.1 and Fig. 6.1.

Needs Assessment

The target population is subdivided into various tumor sites. According to multiple cancer registries, most treated cases will include breast, prostate, lung, and colorectal cancers. Data from Australia [7] indicates that a curative radiotherapy course

Table 6.1	World Cancer Statistics per International Agency for Research on Cancer, World Health
Organizati	ion 2018

Summary statistic 2018			
	Males	Females	Both sexes
Population	3,850,719,284	3,782,099,828	7,632,819,272
Number of new cancer cases	9,456,418	8,622,539	18,078,957
Age-standardized incidence rate (world)	218.6	182.6	197.9
Risk of developing cancer before the age of 75 years (%)	22.4	18.3	20.2
Number of cancer deaths	5,385,640	4,169,387	9,555,027
Age-standardized mortality rate (world)	122.7	83.1	101.1
Risk of dying from cancer before the age of 75 years (%)	12.7	8.7	10.6
5-year prevalent cases	21,014,830	22,826,472	43,841,302
Top 5 most frequent cancers excluding	Lung	Breast	Lung
nonmelanoma skin cancer (ranked by cases)	Prostate	Colorectum	Breast
	Colorectum	Lung	Colorectum
	Stomach	Cervix uteri	Prostate
	Liver	Thyroid	Stomach

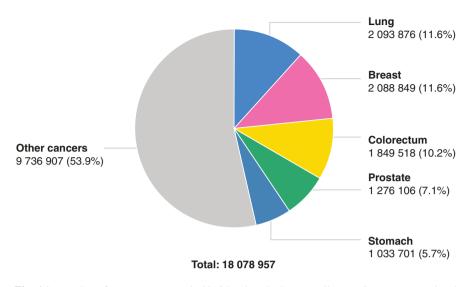


Fig. 6.1 Number of new cancer cases in 2018 by sites, both sexes, all ages. (Source: International Agency for Research on Cancer, World Health Organization 2018)

requires an average of 22 fractions and a palliative course 4 fractions; thus, the total average would be 18 fractions per the first course. The average linear accelerator (linac) treats four to five patients per hour, so the total linac utilization will depend on the total number of hours per day that the machine is active.

In the developed world, most breast cancer (approximately 95%) cases present at potentially curative early stage or locally advanced cases. Evidence of treating breast cases with hypofractionation is well established [8] and widely utilized worldwide.

Similarly, for prostate cancer, due to screening, the majority of cases will present at an early stage (low-risk disease). Treatment options for low-risk prostate cancer include active surveillance (standard of care), radical prostatectomy, external beam radiotherapy, or brachytherapy. It is estimated that 60% of these cases will receive external beam radiation treatment, either definitively or in the early salvage setting, during their disease trajectories. The majority of cases are treated with conventional fractionation (although early salvage radiation usually requires a lower radiation dosage) [9]. Hypofractionation is increasingly an attractive option and often delivered in 20 fractions [10] or fewer. Recently, there is growing evidence of ultra-hypofractionation with seven or fewer fractions that have been utilized in many cancer centers [11].

Lung cancers can be categorized into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), which require different radiotherapy treatment protocols. For NSCLC, stages 1 and 2 comprise 30% of presenting cases, and some of them (medically inoperable) will be treated with curative intent Stereotactic Body Radiotherapy (SBRT). It is estimated that a small percentage will receive SBRT with five or fewer fractions for peripherally located tumors and eight to ten fractions for centrally located one [12]. Approximately, 45% of NSCLC cases present at stage III and are treated with concurrent chemoradiation [13]. For SCLC, which comprises ~15% of all lung cancer cases, both limited and extensive stage presentations are considered. For limited-stage SCLC (33% of cases), the radiation treatment is thoracic radiation with 30 fractions twice daily with at least 6 h apart [14] to follow with prophylactic cranial radiation in 10 fractions [15]. For extensive-stage SCLC (66% of cases), the standard treatment is a systemic therapy, and the responder will require consolidative thoracic radiation with [16] +/– prophylactic cranial radiation [17].

In the category of colorectal cancers, radiotherapy has a more limited role except for rectal cancers, where radiation treatment is often utilized. Rectal cancers comprise of ~28% of colorectal cancers, and ~20% of rectal cancers are metastatic at presentation. The remaining 80% is often treated with long-course chemoradiation [18], which is typical in the neoadjuvant and adjuvant setting. Another alternative is short-course radiotherapy, with five fractions in selected cases.

For endometrial cancer, most cases present at an early stage and need observation or vault brachytherapy in an adjuvant setting. However, assuming at most, 30% of endometrial cancers will require external beam radiation. This includes medically inoperable and adjuvant treatment cases treated with 25 fractions [19]. Approximately 60% of cervical cancers present between stage IB2 and stage IVA and require external beam radiation as part of treatment. The most common prescription is 25 fractions [20]. Approximately 40% of esophageal cancers present at a curable stage, requiring on average concurrent chemoradiation [21].

Palliative cases constitute a significant radiation oncology workload component, and up to 50% of all oncology cases may receive palliative intent treatment. This includes new patients presenting with the metastatic and non-curable disease, and previously treated patients who have developed a non-curable recurrence. The majority of palliative intent treatments constitute radiotherapy for bone metastases, brain metastases, and spinal cord compression. For bone metastases, the most common prescription is single or a few fractions. For spinal cord compression, the most common prescription is ten or fewer fractions. For brain metastases, the main treatment options include fractionated whole-brain radiation or stereotactic radiosurgery (SRS) with single fraction doses ranging from 15 to 24 Gy depending on the target's size [22].

Head and neck cancers and sarcomas typically require the services of surgical oncologists with highly specialized training. There is existing evidence that supports that the outcomes for head and neck cancers [23], sarcomas [24], and bladder cancers [25] are significantly better in tertiary high-volume centers with specialized care in these areas. Similarly, pediatric oncology is highly subspecialized and requires input and management from multiple disciplines.

Brachytherapy

This section focuses on the use of brachytherapy to treat prostate, endometrial, and cervical cancers. For prostate cancer, brachytherapy can be used as monotherapy for low-risk and intermediate-risk patients, or in combination with external beam radiation therapy (EBRT) as a form of dose escalation for selected intermediate-risk and

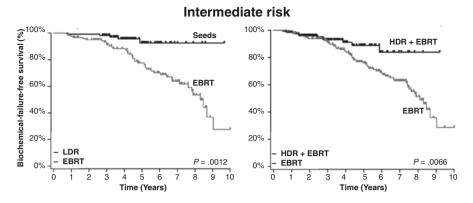


Fig. 6.2 Kaplan-Meier curves comparing propensity score-matched patients receiving external beam radiation therapy (EBRT) versus brachytherapy (BT) for intermediate-risk patients. (Smith et al. [27])

high-risk patients. Brachytherapy with either permanent implants (low dose rate [LDR]) or temporary implants (high dose rate [HDR]) has become an integral component of radiation therapy with excellent oncological outcome [26]. There is well-established evidence suggesting that low and intermediate-risk prostate cancer patients who are treated with brachytherapy have superior outcomes compared to EBRT in terms of better biochemical failure-free survival (e.g., PROCARS Database where 7974 prostate cancer patients managed at four Canadian institutions 1994–2010 Fig. 6.2) [27]. This evidence supports the increased utilization of brachytherapy treatment.

The general rationale for using brachytherapy is as follows:

- 1. Dose escalation is required to maximize cancer control.
- Brachytherapy enables increased dose delivery to the target and sparing of adjacent healthy tissues.
- 3. The low a/β ratio of prostate cancer provides a radiobiological rationale for HDR brachytherapy.
- 4. There is a substantial body of clinical evidence to support the use of prostate brachytherapy.

Many cancer centers plan to use only HDR brachytherapy instead of permanent implants LDR as there is a dosimetric and practical rationale for this. Because dose optimization with HDR brachytherapy is performed after placement of catheters, HDR enables more consistent target coverage and excellent dose uniformity, resulting in a lower dose to the urethra and rectum when compared to permanent seed implants [28]. Currently, there is no clinical evidence to suggest that HDR brachytherapy is inferior to LDR brachytherapy. Thus, offering HDR brachytherapy alone is a costeffective solution without compromising clinical efficacy when resources are limited.

It is estimated that $\sim 13-15\%$ of total prostate cancer patients will eventually receive brachytherapy (LDR or HDR) alone or combined with EBRT. The suggested dose and fractionation schemes are detailed in Table 6.2.

	Single fraction boost (before EBRT)	HDR monotherapy	Focal salvage
Dose fractionation	15 Gy/1 F	19 Gy/1 F (worse outcome) Or 13.5 Gy/2 F (1 week apart)	13.5 Gy/2 F (1 week apart)

Table 6.2 Suggested dose and fractionation for HDR brachytherapy in prostate cancer

Table 6.3 Suggested dose and fractionation for HDR brachytherapy in endometrial cancer

Scenario	External beam dose	HDR dose per fraction	Number of fractions
Adjuvant with EBRT	45 Gy/25	5.5 Gy to 0.5 cm	2
Sole adjuvant	0	7 Gy to 0.5 cm	3
Recurrence with EBRT	45 Gy/25 50.4 Gy/28	7 Gy to 0.5 cm 6 Gy to 0.5 cm	2 2
Recurrence following previous RT	0	7 Gy to 0.5 cm	3

We estimate that a high number of patients will be diagnosed with endometrial cancer. The majority of these cancers are seen in postmenopausal women, with a median age of 60 years. The majority of them will be early stage disease and require surgical intervention with a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). We estimate that at most we will treat one-third with vaginal vault brachytherapy either alone or in combination with external beam radiation therapy. Each patient will require two to three fractions of treatment. Patients are routinely booked for three insertions to allow the additional dose to be given if there is an incomplete response after two insertions.

There are three sets of vaginal vault applicators depending on size (small, medium, and large). Most utilize cylindrical applicators (various diameters (20–40 mm) and lengths (2.5–10 cm)) with a dome cylinder at the top and with one central channel or two to three channels in different configurations. The suggested dose and fractionation schemes are detailed in Table 6.3.

It is well established that HDR brachytherapy is an essential component of cervical cancer management. It has been estimated that 70% of these patients will be candidates for HDR brachytherapy. There is growing evidence that better oncological outcomes can be achieved with the utilization of MRI guidance. As per the consensus of the Brachytherapy in Cervical Cancer Expert Working Group (BCCEWG) Panel of the Cancer Care Ontario (CCO) meeting in 2009 [29], MRI was strongly recommended for delineation of target volumes and planning. The meeting concluded that CT provided acceptable but significantly inferior soft-tissue delineation and, in many cases, could not accurately delineate the target volumes. As per BCCEWG, cervical Brachytherapy also requires that it should only be done at centers with direct access to appropriate gynecological expertise for multidisciplinary patient assessment. The suggested dose and fractionation schemes are detailed in Table 6.4.

		HDR dose per	Number of
Scenario	External beam dose	fraction	fractions
Standard prescription	45 Gy/25 + parametrial boost	5.5 Gy to point A	5
Alternative prescription for patients requiring fewer HDR fractions	45 Gy/25 + parametrial boost	8 Gy to point A	3

Table 6.4 Suggested dose and fractionation for brachytherapy prescription for cervical cancer

Equipment

This section describes the required equipment for delivering both external beam radiation and brachytherapy. A radiotherapy center aiming at treating an average of 1000 patients/year need to be equipped with at least a single-photon energy unit, a brachytherapy afterloader (ideally for high dose-rate brachytherapy), a full range of applicators, a simulator, preferably a CT simulator, a computerized treatment planning system (TPS), patient immobilization devices, and a beam measurement and quality assurance (QA) equipment [30].

External Beam Radiotherapy

For a resource-limited area, the decision to use a cobalt-60 unit or a linear accelerator (linac) for radiotherapy depends on various factors. The use of linacs in developing countries is increasing [31]. With good infrastructure and reliable power supply, a linac is preferred, although curative and effective radiation treatments are possible with a cobalt-60 unit. Linacs can generate electron treatment beams that can be used to treat skin cancers. However, linacs require more frequent quality assurance that needs to be carried out by a medical physicist.

Most newer facilities are equipped with high-energy linacs with intensitymodulated radiation therapy (IMRT), volumetric arc therapy (VMAT), and imageguided radiation therapy (IGRT) capabilities. This will require a careful review of deliverables, functionality, technical specifications, and cost of all commercially available linacs. It is crucial to evaluate the quality of the manufacturer's service and technical support that they will provide.

Linacs will have different energies, with 6 MV photon beams and 15–18 MV photon beams as the more commonly used energies. There is no anticipated need for 25 MV capability because the uniformity produced by 18 MV photons over targets is generally deemed sufficient while yielding less neutron production and, therefore, requiring less shielding. Further, some manufacturers no longer provide a 25 MV photon beam as a standard option. Installing a linac with 25 MV photons will only increase the price of the unit with no anticipated great benefit for the clinic. Stereotactic radiation and ablative treatments can be performed on the linac, Gamma

Knife, or Cyberknife systems. There will be a need for a CT simulation unit which can be shared between the external beam radiation and brachytherapy programs.

Brachytherapy

There will be a need for a dedicated HDR brachytherapy suite with a treatment room and control area. The brachytherapy treatment room contains a mini operating theatre equipped with the following:

- A Remote afterloader
- · An in-room radiation detector and check source
- · Audiovisual communication systems
- · A securely locked door and door interlock
- · A multiple-position patient procedure table
- A mobile ultrasound machine for guidance
- · Emergency crash cart and recovery equipment
- Survey meter
- · An anesthesia area with patient monitoring equipment
- An operating room procedure light
- A sink and scrub area
- · Emergency shut-off buttons

Both Co-60 and Ir-192 are commonly used as sources in HDR brachytherapy; however, Ir-192 is usually selected as the radiation source to be used for the remote afterloader system due to lower photon energy and advantages it offers with regard to radiation protection. For example, the use of Ir-192 results in the amount of concrete required to be cut in half compared to Co-60.

An adjacent control area will allow for safe monitoring of the brachytherapy procedure and patient. Cameras will be needed for patient observation. Intercom facilities between the treatment room and control area are required to permit direct communication with the patient during the treatment. There will be dedicated computers and planning workstation in the control room.

Recovery area [32, 33]

- One anesthesiologist need to be present in the facility until such time that the last surgical patient of the day is deemed fully conscious.
- A fully qualified registered two nurses need to be present in the room. They must know and be in charge of the equipment, critical supplies, personnel assignments, and duties.
- Two fully equipped recovery beds. There should be curtains or screens to allow privacy.
- Space allocated per bed/trolley should be at least 9 m². There must be easy access to the patient's head.
- Adequate space to allow the transport of patients and movement of personnel. A continuous oxygen delivery system must be in place.

- All necessary medical equipment from monitoring, suction, and resuscitation equipment must be available.
- The emergency power source must be available, which will provide adequate lighting essential area lighting, and have the capacity to operate all necessary equipment.

Commissioning

Once the equipment is acquired from vendors, it will be subject to acceptance testing where tests and measurements will be performed to ensure that the equipment of software meets the specifications set by the manufacturer. The manufacturer will indicate the acceptance testing protocol, and the testing process will be jointly carried out by the installation technicians and medical physicists. Each facility needs to have the necessary equipment for acceptance testing, which might include: a 3D water phantom scanner, ion chambers, electrometer X-ray films, and film laser scanner. The American Association of Physicists in Medicine (AAPM) makes available useful task group reports (TG-35, TG-40, and TG-43) that provide detailed information about linacs safety and quality assurance.

Room Shielding

Design of the radiation treatment room shielding incorporated consideration of As Low As Reasonably Achievable (ALARA) principles, International Atomic Energy Agency (IAEA) Safety Standard Series, National Council on Radiation Protection and Measurements (NCRP), and American Association of Physicists in Medicine (AAPM) corresponding reports and the requirements set by different Safety Commissions, which mandates the maximum allowed limits of radiation exposure to occupants adjacent to the treatment rooms. These limits depend on whether or not those occupants would be considered nuclear energy workers (e.g., radiation therapists) or members of the public (e.g., patient family members, administrative staff). Important factors influencing the room shielding requirements and, therefore, corresponding cost include but are not limited to the expected workload of the unit (output in dose (Gy) per year), maximum expected dose rates per fraction, conventional or specialized treatment protocols, and associated fractionation (e.g., stereotactic body radiation therapy (SBRT)) and a number of palliative fractions and expected dose.

Careful selection of treatment room placement can help save cost by aligning the rooms such that walls requiring more shielding are shared (e.g., primary walls) and preventing most walls from being adjacent to public areas (e.g., by having the bunkers underground where some walls are lined by the earth and having treatment areas aligned such that most do not border a public waiting area).

Radiotherapy Staffing

The core professional team in radiotherapy consists of radiation oncologists, radiation therapists, dosimetrists, and medical physicists supported by nursing, administration, and various medical officers.

Personnel

To best serve the population, and based on the proposed size of the facility with linacs and brachytherapy unit, we can anticipate the need for radiation oncologists (ROs). According to the Cancer Care Ontario (CCO), the number of ROs required at any radiation center is consistent regardless of the size of the center and is 1.8–2 ROs per linac. Many community radiation centers operated within that framework. To run the linacs and an additional brachytherapy unit, we propose using a factor of two ROs per linac. A 0.5 Full-Time Equivalent (FTE) anesthesiologist is required for Brachytherapy, and 1 FTE medical oncologist for concurrent chemoradiation.

Based on the proposed number of concurrent clinics, we also anticipate the need for a number of dedicated nurses. Those would be used to see patients coming for clinic appointments, for radiation review clinic, for the brachytherapy unit, to take calls from patients and other healthcare providers, to run the chemotherapy suite, and float nurses. There will be a need for clinic coordinators to help with patient flow. The facility will need radiation therapists to help run the facility. Generally, four therapists are needed per linac. Two would be required to run the CT sim and two more for the brachytherapy suite. An additional dosimetrist would be dedicated to radiation planning.

Other support staff required would include administrative assistants for the ROs, administrative assistants to check patients in for CT sim or radiation treatments, and janitorial staff.

Quality Assurance

The responsibility for quality assurance and safety falls on every individual working at the radiotherapy facility, including radiation therapists, physicists, and radiation oncologists. In this section, some of the planned quality assurance activities for radiation oncologists and physicists will be discussed.

Physics: Equipment-specific quality assurance will be performed on all treatment equipment and software. Regular and continuous QA testing for equipment will be necessary to ensure safe and correct functioning. A written equipment quality control program must specify the required policies and procedures:

- 1. Parameters to be tested or the tests to be performed
- 2. Instruments to be used to perform the tests
- 3. Test setup (geometry, etc.)
- 4. Frequency of the tests
- 5. Individuals responsible for testing
- 6. Expected results or values
- 7. Tolerance level
- 8. Action to be taken when tolerance is exceeded

QA procedures for treatment machines will be performed on a daily, monthly, and annual basis using the guidelines and recommendations specified in the TG-45 report "AAPM code of practice for radiotherapy accelerators: Report of AAPM Radiation Therapy Task Group No. 45". The radiation therapists will perform daily machine QA, whereas the monthly and annual QA procedures will be the responsibility of the physicists. QA will mandate compliance with the specific requirements for remote afterloading units of the HDR brachytherapy unit.

Physicists will also be responsible for "chart checks" before delivery of 20% of the total dose, where a review of the prescription and treatment plan will be performed along with an independent MU calculation. There will also be a weekly physics chart check to ensure that the treatment is delivered as intended.

Oncologists: Oncologists will participate in weekly tumor board conferences where there will be input from surgeons and medical oncologists, and other medical doctors for the management of difficult or challenging cases. Usually, each site will require two oncologists' practice in that specific area, so that peer review of plans can be performed. Each section will have dedicated weekly quality assurance rounds where this process can take place. Usually, the quality assurance rounds will require the presence of at least two oncologists, one physicist, and two radiation therapists.

Timeline

A typical timeline of approximately a few years from the time of approval to the time when patients can first be treated is reasonable. The proposed timeline would break down as follows:

- 1. Commissioning design, engineering firms, architectural plans (6–12 months)
- 2. Facility and bunker construction (1–2 years)
- 3. Install linacs, CT, brachytherapy equipment (6–12 months)
- 4. Get clinic space up and running (3–6 months)
- 5. Training for ROs, physicists, planners (3–6 months)

Parameter	Low end	High end
HDR device	\$250K	\$350K
Applicator	\$50K	\$100K
OR table	\$35K	\$75K
Vault	\$40K	\$80K
US	\$20K	\$75K
Anesthesia	\$50K	\$100K
Planning system	\$150K	\$200K
Construction	\$50K	\$70K

Table 6.5 Estimation of the cost of brachytherapy suite (please note as these values might vary significantly depending on regions)

Table 6.6 Staffing costs for the proposed radiation therapy facility (please note as these values might vary significantly depending on regions)

Staff	Cost per FTE (\$)
Radiation oncologists	180,000
Other physicians (anesthesia, medical oncology)	180,000
Physicists	135,000
Nursing	65,000
Radiation therapists	80,000
Information technologists	80,000
Administrative assistants	50,000
Janitorial staff	30,000

Budget

The anticipated life span of technology is 10 years. The brachytherapy suite costs are estimated in Table 6.5.

In terms of personnel, the estimated salaries are drawn from the literature from Europe and converted to dollars [34]. Note that base salaries are included for radiation oncologists and not the fee for service aspect. The staffing costs are estimated in Table 6.6.

Conclusion

Establishing a new radiotherapy facility is a complicated and costly process that required careful planning, understanding of the local disease burden, infrastructure, and multimodality expertise. Each step has many obstacles and challenges. The people, time, and money commitment can be substantial but rewarding and reduce cancer patients' suffering.

References

- 1. Farmer P, Frenk J, Knaul FM, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. Lancet. 2010;376:1186–93.
- Barton MB, Frommer M, Shafiq J. Role of radiotherapy in cancer control in low-income and middle-income countries. Lancet Oncol. 2006;7:584–95.
- Delaney GP, Barton MB. Evidence-based estimates of the demand for radiotherapy. Clin Oncol (R Coll Radiol). 2015;27:70–6.
- 4. International Atomic Energy Agency (IAEA). Radiotherapy facilities: master planning and concept design considerations. IAEA Human Health Reports No. 10. 2014.
- Efstathiou JA, Heunis M, Karumekayi T, Makufa R, Bvochora-Nsingo M, Gierga DP, Suneja G, Grover S, Kasese J, Mmalane M, Moffat H, von Paleske A, Makhema J, Dryden-Peterson S. Establishing and delivering quality radiation therapy in resource-constrained settings: the story of Botswana. Oncologia. 2016;34(1):27–35. https://doi.org/10.1200/JCO.2015.62.8412.
- Zubizarreta EH, Fidarova E, Healy B, Rosenblatt E. Need for radiotherapy in low and middleincome countries – the silent crisis continues. Clin Oncol (R Coll Radiol). 2015;27:107–14.
- IIAMR and CCORE. Review of optimal radiotherapy utilisation rates. Liverpool, NSW: Ingham Institute for Applied Medical Research (IIAMR) – Collaboration for Cancer Outcomes Research and Evaluation (CCORE); 2013.
- Whelan TJ, Pignol J-P, Levine MN, Julian JA, MacKenzie R, Parpia S, Shelley W, Grimard L, Bowen J, Lukka H, Perera F, Fyles A, Schneider K, Gulavita S, Freeman C. Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med. 2010;362(6):513–20.
- Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, Davis M, Peters TJ, Turner EL, Martin RM, Oxley J, Robinson M, Staffurth J, Walsh E, Bollina P, Catto J, Doble A, Doherty A, Gillatt D, Kockelbergh R, Kynaston H, Paul A, Powell P, Prescott S, Rosario DJ, Rowe E, Neal DE, ProtecT Study Group. 10-Year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med. 2016;375(15):1415–24.
- Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, Graham J, Kirkbride P, Logue J, Malik Z, Money-Kyrle J, O'Sullivan JM, Panades M, Parker C, Patterson H, Scrase C, Staffurth J, Stockdale A, Tremlett J, Bidmead M, Mayles H, Naismith O, South C, Gao A, Cruickshank C, Hassan S, Pugh J, Griffin C, Hall E, CHHiP Investigators. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomized, non-inferiority, phase 3 CHHiP trial. Lancet Oncol. 2016;17(8):1047–60.
- 11. Jackson WC, Silva J, Hartman HE, Dess RT, Kishan AU, Beeler WH, Gharzai LA, Jaworski EM, Mehra R, Hearn JWD, Morgan TM, Salam SS, Cooperberg MR, Mahal BA, Soni PD, Kaffenberger S, Nguyen PL, Desai N, Feng FY, Zumsteg ZS, Spratt DE. Stereotactic body radiation therapy for localized prostate cancer: a systematic review and meta-analysis of over 6,000 patients treated on prospective studies. Int J Radiat Oncol Biol Phys. 2019;104(4):778–89. https://doi.org/10.1016/j.ijrobp.2019.03.051.
- Timmerman RD, Hu C, Michalski JM, Bradley JC, Galvin J, Johnstone DW, Choy H. Longterm results of stereotactic body radiation therapy in medically inoperable stage I non-small cell lung cancer. JAMA Oncol. 2018;4(9):1287–8. https://doi.org/10.1001/jamaoncol.2018.1258.
- 13. Bradley JD, Paulus R, Komaki R, Masters G, Blumenschein G, Schild S, Bogart J, Hu C, Forster K, Magliocco A, Kavadi V, Garces YI, Narayan S, Iyengar P, Robinson C, Wynn RB, Koprowski C, Meng J, Beitler J, Gaur R, Curran W Jr, Choy H. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a rerandomized two-by-two factorial phase 3 study. Lancet Oncol. 2015;16(2):187–99. https://doi.org/10.1016/S1470-2045(14)71207-0. Epub 2015 Jan 16.
- 14. Turrisi AT 3rd, Kim K, Blum R, Sause WT, Livingston RB, Komaki R, Wagner H, Aisner S, Johnson DH. Twice-daily compared with once-daily thoracic radiotherapy in limited

small-cell lung cancer treated concurrently with cisplatin and etoposide. N Engl J Med. 1999;340(4):265-71.

- Aupérin A, Arriagada R, Pignon JP, Le Péchoux C, Gregor A, Stephens RJ, Kristjansen PE, Johnson BE, Ueoka H, Wagner H, Aisner J. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial Irradiation Overview Collaborative Group. N Engl J Med. 1999;341(7):476–84.
- 16. Slotman BJ, van Tinteren H, Praag JO, Knegjens JL, El Sharouni SY, Hatton M, Keijser A, Faivre-Finn C, Senan S. Use of thoracic radiotherapy for extensive-stage small-cell lung cancer: a phase 3 randomized controlled trial. Lancet. 2015;385(9962):36–42. https://doi.org/10.1016/S0140-6736(14)61085-0. Epub 2014 Sept 14.
- Slotman B, Faivre-Finn C, Kramer G, Rankin E, Snee M, Hatton M, Postmus P, Collette L, Musat E, Suresh S, EORTC Radiation Oncology Group and Lung Cancer Group. Prophylactic cranial irradiation in extensive small-cell lung cancer. N Engl J Med. 2007;357(7):664–72. https://doi.org/10.1056/NEJMoa071780.
- Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, Martus P, Tschmelitsch J, Hager E, Hess CF, Karstens J-H, Liersch T, Schmidberger H, Raab R, German Rectal Cancer Study Group. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2004;351(17):1731–40. https://doi.org/10.1056/NEJMoa040694.
- Creutzberg CL, Nout RA, Lybeert MLM, Wárlám-Rodenhuis CC, Jobsen JJ, Mens J-WM, Lutgens LCHW, Pras E, van de Poll-Franse LV, van Putten WLJ, PORTEC Study Group. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. Int J Radiat Oncol Biol Phys. 2011;81(4):e631–8. https://doi.org/10.1016/j. ijrobp.2011.04.013. Epub 2011 June 2.
- Landoni F, Colombo A, Milani R, Placa F, Zanagnolo V, Mangioni C. Randomized study between radical surgery and radiotherapy for the treatment of stage IB-IIA cervical cancer: 20-year update. J Gynecol Oncol. 2017;28(3):e34. https://doi.org/10.3802/jgo.2017.28.e34. Epub 2017 Feb 24.
- 21. Joel S, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, van Laarhoven HWM, Nieuwenhuijzen GAP, Hospers GAP, Bonenkamp JJ, Cuesta MA, Blaisse RJB, Busch ORC, Ten Kate FJW, Creemers G-JM, Punt CJA, Plukker JTM, Verheul HMW, Spillenaar Bilgen EJ, van Dekken H, van der Sangen MJC, Rozema T, Biermann K, Beukema JC, Piet AHM, van Rij CM, Reinders JG, Tilanus HW, Steyerberg EW, van der Gaast A, CROSS Study Group. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol. 2015;16(9):1090–8. https://doi.org/10.1016/ S1470-2045(15)00040-6. Epub 2015 Aug 5.
- 22. Shaw E, Scott C, Souhami L, Dinapoli R, Kline R, Loeffler J, Farnan N. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05. Int J Radiat Oncol Biol Phys. 2000;47(2):291–8. https:// doi.org/10.1016/s0360-3016(99)00507-6.
- Corry J, Peters LJ, Rischin D. Impact of center size and experience on outcomes in head and neck cancer. J Clin Oncol. 2015;33(2):138–40. https://doi.org/10.1200/JCO.2014.58.2239.
- 24. Bonvalot S, Miceli R, Berselli M, Causeret S, Colombo C, Mariani L, Bouzaiene H, Le Péchoux C, Casali PG, Le Cesne A, Fiore M, Gronchi A. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. Ann Surg Oncol. 2010;17(6):1507–14.
- Hollenbeck BK, Wei Y, Birkmeyer JD. Volume, process of care, and operative mortality for cystectomy for bladder cancer. Urology. 2007;69(5):871–5. https://doi.org/10.1016/j. urology.2007.01.040.
- Keyes M, Crook J, Morris WJ, Morton G, Pickles T, Usmani N, Vigneault E. Canadian prostate brachytherapy in 2012. Can Urol Assoc J. 2013;7(1–2):51–8. https://doi.org/10.5489/cuaj.218.
- 27. Smith GD, Pickles T, Crook J, Martin AG, Vigneault E, Cury FL, et al. Brachytherapy improves biochemical failurefree survival in low- and intermediate-risk prostate cancer compared with

conventionally fractionated external beam radiation therapy: a propensity score matched analysis. Int J Radiat Oncol Biol Phys. 2015;91:505–16.

- Wang Y, Sankreacha R, Al-Hebshi A, et al. Comparative study of dosimetry between highdose-rate and permanent prostate implant brachytherapies in patients with prostate adenocarcinoma. Brachytherapy. 2006;5:251–5.
- 29. Morton G, Walker-Dilks C, Baldassarre F, et al. The delivery of brachytherapy for cervical cancer: organizational and technical advice to facilitate high-quality care in Ontario: guideline recommendations. Report Date: November 11, 2009.
- 30. Rosenblatt E. Planning national radiotherapy services. Front Oncol. 2014;4:315.
- Page BR, Hudson AD, Brown DW, et al. Cobalt, linac, or other: what is the best solution for radiation therapy in developing countries. Int J Radiat Oncol Biol Phys. 2014;89:476–80.
- 32. Canadian Association for Accreditation of Ambulatory Surgery Facilities. Criteria for Accreditation of Ambulatory Surgical Facilities.
- Australian and New Zealand College of Anaesthetists Recommendations for the Post-Anaesthesia Recovery Room.
- Peeters A, Grutters JPC, Pijls-Johannesma M, et al. How costly is particle therapy? Cost analysis of external beam radiotherapy with carbon-ions, protons and photons. Radiother Oncol. 2010;95(1):45–53.

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