

Review Article

Brachytherapy: An Emerging Science or Demise in Quiet?

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Abstract

Brachytherapy consists of placing radioactive sources within or directly adjacent to the tumor to deliver a highly conformal radiation dose in the shortest possible time. It aims to sculpt the optimal isodose on the tumor volume while sparing normal tissues. The benefits are fourfold: patient cure, organ preservation, time sparing and cost-efficiency. Despite these benefits, brachytherapy is lacking its vitality in the modern era. Except for a handful of centers, the majority of hospitals & research institutions have non-functional or minimally functional brachytherapy units hence obscuring the patients & young radiation learners from the unmatched benefits of this curative treatment modality.



This article looks into the various aspects of brachytherapy in India & abroad: from its beginning to the present day. It points out the various advances made in brachytherapy to match the current teletherapy practices, evidence in support of its decline, reasons for its fall, and some possible solutions to make this field more popular & continuously evolving.

KEYWORDS: *Teletherapy, Image-guided Brachytherapy, Accelerated Partial Breast Irradiation (APBI), Brachytherapy.*

Introduction

Brachytherapy was the first radiotherapy modality used for the treatment of cancer patients, much before the first teletherapy machine was invented. In the early 20th century, this fine art evolved under the guardianship of stalwarts like *Madam Curie, Paterson, Parker, Fletcher, Deutrix*, to name a few. Since its inception in 1895, constant technological advances have driven Brachytherapy. We have evolved from radium to iridium, from manual loading to remote after loading, from LDR (low dose rate) to HDR (high dose rate), from X-ray to CT-MRI-based planning & advanced dose calculation & optimization tools. These advances have made the brachytherapy treatment more efficient & well tolerated to preserve function, cosmesis, and quality of life, together with the potential to realize lower utilization of health care resources and associated costs. Various randomized trials in different types of cancer (including head & neck, cervix, breast, prostate and many more) have exhibited the safety & efficacy of Brachytherapy with a high level of scientific evidence.

However, such achievements, of major importance for the treatment & cure of cancer patients, were neglected during the past decade by technology-driven modern EBRT (external beam radiotherapy) techniques & computer-savvy generation. Teletherapy has made phenomenal strides that have seemingly buoyed radiation oncology to a superfast and supersonic era. More recently, these developments were further suppressed by barging in of hoax data of market-driven clinical researches on proton and particle beam therapy, newer chemotherapy and targeted therapy without achieving much clinical benefit as was seen during the brachytherapy era.

This article reviews the timeline of 100 years of radiotherapy with a focus on breakthroughs in the field of brachytherapy physics, technology & applications during the past two decades, and the associated clinical benefits along with the recent disturbing reports and trends of an alarming decline in the utilization of brachytherapy worldwide. It also addresses some of the strategies to bring back the lackluster of this unique form of radiotherapy, which involves art, science, skill, and judgment: all that



is called for to stand out in the competent & challenging world of oncology practice.

History of Brachytherapy

Brachytherapy is not a new technique. If we explore the illustrious history of radiotherapy, it started in the form of brachytherapy & since then it has been around for over 100 years. Many of our technological discoveries are distinctly marked & credited in history [1, 2, 3]. The first medical experiences of radiotherapy belong to *Danlos & Bloch* in 1901 of Paris and *Abbey* in 1904 of New York for the treatment of skin cancers. The Radium Biological Laboratory was established in Paris in 1906, and *Finze* in London started treatments of cancer with radium in 1909. Initially, the brachytherapy applications were mostly led by clinical observations and from experiences; rules were developed to avoid errors that lead to systems or schools. The basic rules & principles of Radium-226 use in Brachytherapy were established after World War I in medical institutes such as the Radium Hemet in Stockholm, the Memorial Hospital in New York, and the Radium Institute in Paris. For intracavitary treatments, the Stockholm and Paris Methods were developed in 1914 and 1919, respectively & Paterson and Parker set the basis of the 1930 rules for the Manchester System, which was extensively described in a book by Meredith [4].

Two other steps are important to date in the development of brachytherapy. First, is the Discovery of Artificial Radioactivity in 1934, allowing the use of artificial radioactive materials in radiotherapy hence newer radionuclides like Cobalt-60, Cesium-137, and Gold-198 were applied with designs initially similar to Radium-226 sources. Secondly, in the fifties and sixties of the twentieth century, the development of remote after loading devices by *Henschke & Dalcos* allowed improved personnel radiation protection and gave more flexibility to the brachytherapy applications. The next few decades were witness to the development and continuous refinements in applicator design and dosimetry methods.

Recent Advances in Brachytherapy

Brachytherapy has evolved over many decades, but more recently, there have been significant revolutions in the way brachytherapy is practiced for different treatment sites. Latest applicator designs & modern radioactive sources along with advanced imaging, three-dimensional reconstruction algorithms, sophisticated optimization tools, and inverse planning modules; all have modernized brachytherapy, allowing accurate radiation dose delivery to the target with a minimal dose to the surrounding normal critical tissue.

Development of new radioactive sources

In the nineteen-thirties, before the advent of planning computers, treatment planning was mostly carried out by simply following the Manchester system using radium sources [5,6]. An increase in radiation



safety awareness in the nineteen-seventies and nineteen-eighties led to a decline in the use of radium in favor of the relatively newer and safer radioisotopes such as Iridium-192. Since then the introduction of artificially produced radioactive isotopes gave a new dimension, leading to the renaissance of brachytherapy. Newer radionuclides such as Cobalt-60, Cesium-137, Iodine-131, Gold-198 that might be used as radium substitutes were rapidly introduced in the clinic.

Advanced imaging & treatment planning

The use of two-dimensional (2D) imaging remained integral to treatment planning for many years, despite its limitations such as the inability to report any specific dose-volume information for the tumor or organs at risk (OARs). More recently, however, significant advances have resulted in the use of newer imaging modalities, acquiring a three dimensional (3D) data set using computed tomography (CT) and/or magnetic resonance imaging (MRI) has enabled more accurate planning and better dose determination to volumes of both the tumor and the OARs [7]. Technological advances in the form of afterloading techniques and the wider implementation of computerized planning using planar radiographic imaging are implemented in an attempt to verify the applicator or catheter positions and calculate patient-specific dose. Very recently treatment techniques involving online planning have emerged, allowing dose distributions to be calculated and updated in real-time based on the actual clinical situation. In much, the same way that intensity-modulated radiotherapy (IMRT) has advanced the way external beam radiotherapy (EBRT) is planned and delivered, so too have 3D-image-guided and planning optimization techniques have advanced the field of brachytherapy [8].

Standardization of treatment

Alongside these advances, the need to compare patients' treatments at one center with those from other treatment centers was recognized, as an important scientific standardization of treatment. The International Commission on Radiation Units and Measurements (ICRU) reports thirty-eight and fifty-eight details the dose and volume specification required for intracavitary therapy in gynecology and interstitial therapy, respectively. Together, these advances set the stage for a dramatic shift in both clinical indications and technical practice of Brachytherapy that have occurred in the last 15 years.

Advanced brachytherapy treatment in different cancer sites

There are many clinical sites treated with brachytherapy, including regions of the head and neck, bronchus, esophagus, breast, prostate, various gynecological sites, rectum, anus and surface lesions. Some of these treatment sites have witnessed major advances over the past decade which will be discussed here.



Carcinoma Breast: The brachytherapy technique for treating carcinoma breast that has developed over recent years is accelerated partial breast irradiation (APBI). Breast HDR Brachytherapy represents one technique to deliver partial breast irradiation and is the partial breast irradiation technique, with the strongest and longest data supporting its use.

Many international trials have shown comparable outcomes and reduced toxicities with APBI when compared to conventional whole breast irradiation [9,10,11]. Cosmetic outcomes are also improved with brachytherapy. Additionally, HDR brachytherapy can be delivered with multiple techniques based on the patient's anatomy and disease characteristics, allowing for a more patient-specific treatment option. Several innovative treatment delivery methods like multicatheter interstitial implant, balloon catheter brachytherapy like Mammosite & Contura and Hybrid brachytherapy devices like strut-adjusted volume implant (SAVI) and Clear Path have emerged for APBI and have been reviewed by Njeh et al [12].

Carcinoma Prostate: A current area of interest for using high dose rate (HDR) techniques within the prostate is that of focal boosts [13]. In addition to the standard practice of delivering the prescribed dose to the whole prostate, an additional boost dose is given to the dominant intraprostatic lesion (DIL), the region where tumor recurrence is more likely to occur. With advances in high-tech multiparametric magnetic resonance imaging (mp-MRI) methods, such as MR spectroscopy and dynamic contrast-enhanced MRI together with diffusion-weighted MRI, sensitivity, and specificity of prostate cancer detection have improved greatly. Studies have shown that tumor delineation using advanced imaging techniques has successfully enabled a boost dose to the DIL of up to 150% of the prescription dose [14].

Carcinoma Cervix: With the widespread acceptance of CT and MRI in EBRT, a study published in 2007 by a group in Vienna, investigated the clinical impact of MRI-based cervix brachytherapy combined with external beam chemo-radiation [15]. The results showed that with 3D MRI-based planning, local control of more than eighty-five percentage could be achieved with low treatment-related morbidity, i.e grade three/four toxicity of 6% only, as compared to 13% when using simple two dimensional (2D) planning methods. They suggested that for locally advanced disease, the MRI-based approach will likely result in excellent local control (≥ 95 percentage) and minimize treatment-related morbidity. The clear benefit of 3D planning is that there is a potential to optimize the dose to the outlined tumor volume, while maintaining acceptable doses to the OARs, thereby reducing the long-term toxicity. Besides, the traditional point A dose is a poor surrogate of the high-risk clinical target volume (HRCTV) dose and that MRI-based image-guided brachytherapy (IGBT) significantly improves target coverage and organ at risk dose [16,17,18].



Declining trends vs compelling evidence supporting Brachytherapy

Over recent years, there has been an alarming decline in the utilization rates of Brachytherapy internationally. Young radiation oncologists are over thrilled by the plethora of sophisticated computer tools available in modern teletherapy machines that they often forget the central role that brachytherapy continues to play in the management of several cancer types. Some of the published literature on waning usage of brachytherapy along with compelling pieces of evidence supporting brachytherapy are discussed below.

Prostate cancer

In prostate cancer, Martin et al exhausted the National Cancer Data Base to study approximately 1.5 million patients treated between 1998 and 2010. They found that brachytherapy usage reached a peak of 17% in 2002 and steadily declined to as low as 8% in 2010 [19]. Similarly, Mahmood et al used the Surveillance, Epidemiology, and End Results (SEER) database to study approximately 182,000 patients treated between 2004 and 2009 and found that prostate brachytherapy procedures decreased from 44% in 2004 to 38% in 2009. Concurrently, the use of EBRT rose from 11.6% in 2004 to 24.0% in 2009. It was also comprehended that the most dramatic decline in brachytherapy procedures was seen at academic centers (48%), along with a comprehensive community (41%) and community cancer centers (30%) [20].

The reports of declined use of brachytherapy for the treatment of prostate cancer are sad and worrying because an abundance of data has been published demonstrating the undeniable efficacy of the treatment, quality of life, and cost-effectiveness. We have ample evidence where brachytherapy has shown superior biochemical control, local control, low prostate cancer-specific death, when used alone in low-risk prostate cancer or combination with EBRT in higher-risk cancers, compared with surgery or EBRT alone [21]. A noteworthy study by a multi-institutional group of prostate cancer experts concluded that men with high-risk prostate cancer treated with external beam radiation therapy (EBRT), brachytherapy seed implant and hormone deprivation therapy, were associated with significantly better prostate cancer-specific mortality rates (*deaths caused by prostate cancer*) compared to radical prostatectomy or EBRT with hormone deprivation therapy [22].

Additionally, researchers from the British Columbia Cancer Agency, published a landmark, Level 1 evidence trial, that concluded men with Intermediate & High-Risk prostate cancer randomized to low-dose brachytherapy boost, EBRT, and hormone deprivation (versus men randomized to EBRT boost, EBRT, and hormone deprivation therapy) were twice as likely to be free of biochemical failure (detectable and rising **Prostate-Specific Antigen (PSA)**) at a median follow-up of 6.5 years[23]. This is despite the universal fact that compared with candidates for RP, patients who are offered radiotherapy generally



tend to be older and have higher comorbidity and more aggressive cancer-associated risk features, such as initial PSA, clinical stage, percentage of positive biopsy, etc. Unfortunately, many men diagnosed with prostate cancer are never presented with Prostate Brachytherapy Seed Implants as a treatment option and/or, more regrettably, presented with misinformation. Petereit et al. suggested few reasons for this decline such as increased use of robotic prostatectomies and EBRT preferred by radiation oncologists because of advances such as Image-Guided Radiotherapy (IGRT), Stereotactic Ablative Body Radiotherapy (SABR) and also negative press reports of poor quality implants [24]. When given choice to the patients, then also IMRT is preferred because of being non-invasive & reimbursable by insurance companies. Even nations like the United States have limited brachytherapy facilities leading to restricted opportunities for training and experience and are therefore less likely to refer patients for brachytherapy.

Carcinoma cervix

The situation for treatments for cancer of the cervix is a little more upsetting. From the SEER database, Han et al. found 7359 patients with stages IB2-IVA cervical cancer treated with EBRT between 1988 and 2009 & noted a decline in the utilization of brachytherapy for cervix cancer from 83 % in 1988 to 58 % in 2009, noting a particular dip in the utilization in 2003 which happened to coincide with the introduction of a healthcare rebate for intensity-modulated radiotherapy (IMRT) in the United States [25].

More recently, Gill et al used the National Cancer Data Base to analyze various radiation dose-escalation techniques that were used in the treatment of 7,654 patients with cervical cancer [26]. From 2004 to 2011, the use of brachytherapy decreased from 96.7% to 86.1% whereas the use of IMRT and stereotactic body radiotherapy (SBRT) increased from 3.3% to 13.9%. The median survival time was 70.9 months for patients who received brachytherapy compared with 47.1 months for those dose-escalated with either IMRT or SBRT as an alternative to brachytherapy. The risk of cervical cancer-specific death was significantly higher for women who did not receive brachytherapy despite controlling for several relevant clinical and pathologic factors. Of particular note, the increase in the mortality rate was significantly prominent for patients who did not receive brachytherapy than for those who did not receive chemotherapy.

The Quality Research in Radiation Oncology study reviewed the records of 261 randomly selected patients from 45 institutions who received radiation for cervical cancer from 2005 to 2007 and compared them to patients treated in the period from 1996 to 1999 [27]. One of the key findings was that 13% of patients treated from 2005 to 2007 did not receive brachytherapy, almost double the rate that was noticed in the earlier cohort. Hence, it was concluded that not all centers worldwide offer a brachytherapy service and even those that do, the range of practices varies, and caseloads are not high



in all but a few centers.

This is despite significantly higher rates of cause-specific survival and overall survival in patients treated with brachytherapy. A noteworthy study of over 7,000 patients with non-operable, locally advanced cervical cancer treated with radiation therapy between 1988 to 2009 found that patients who received HDR GYN (Gynecological) Brachytherapy as part of their cancer treatment had higher rates of survival than patients who received external beam radiation alone [25]. At 4 years after treatment, the survival rate was 12% higher in patients receiving brachytherapy. Furthermore, researchers reported the results of a large patient study of non-operable, locally advanced cervical cancer patients treated in the United States between 2004 to 2011, who sought to evaluate the impact that different types of "boost" radiation have on treatment outcomes [26]. The researchers found better cure rates in patients treated with HDR GYN Brachytherapy compared to other types of "boost" radiation therapy and concluded that HDR GYN Brachytherapy remains a critical treatment component for non-operable, locally advanced cervical cancer. Hence we can infer that the reports of the declining trend of brachytherapy applications are universal. The decline is alarming; when we consider that there is compelling evidence that Brachytherapy, in appropriately selected patients, is capable of accurately delivering a highly conformal dose of radiation to the tumor and lower doses to surrounding healthy tissue compared with modern external beam radiotherapy techniques (intensity-modulated radiotherapy-IMRT, image-guided radiotherapy-IGRT, stereotactic surgery-SRS, stereotactic body radiotherapy SBRT). Also, the majority of times the use of brachytherapy has led to better local control rates, improved overall survival, minimum morbidity, and functional/cosmetic loss. Despite this, it seems to be losing referrals to EBRT colleagues who claim that with exciting advances in technology, there are increasing opportunities for modern EBRT techniques to safely deliver tightly conformal fields of radiation in a small number of fractions...something being done in Brachytherapy for many years!

Indian scenario

India is a developing nation with a huge cancer burden and a lack of upgraded radiation oncology equipment and an expert workforce for highly conformal treatment hence brachytherapy can be extremely useful and effective to deliver the curative dose. However, for some reason, brachytherapy is not utilized to its full potential in India [28]. Barring a few institutes, most of the other Government-run state hospitals and medical colleges lack infrastructure & trained professionals. The latest developments in brachytherapy such as the incorporation of MRI & Positron emission tomography (PET), improved brachytherapy applicators, new planning systems, etc. have been successfully implemented in the developed world however, their implementation and wide practice in India is a big future dream. On one end brachytherapy units in India, are lacking up-gradation & on the other end, corporate and private hospitals advertise and push for advanced radiation techniques like IMRT and IGRT, and not



brachytherapy because brachytherapy treatments are not a priority for reimbursements. Hence, the practice of brachytherapy in India faces additional challenges leading to a decline in its usage.

Robust reasons For Promotion of This Old Art

Brachytherapy delivers the ultimate form of conformal radiotherapy. As of now, this technique remains unmatched in its sharp fall-off and precision in its treatment delivery. Several pioneering publications in various body sites have shown Brachytherapy to be superior to its congener radiotherapy tools in achieving conformity & better clinical outcome. Let us discuss a few sites that have witnessed how brachytherapy has changed the definition of conformal radiotherapy.

Prostate Cancer

The range of imaging tools now used in real-time has greatly expanded the possibilities of brachytherapy. In prostate cancer & many other cancer sites, advances in high-tech multiparametric MRI (mp-MRI) methods, such as MR spectroscopy and dynamic contrast-enhanced MRI have increased the sensitivity and specificity of tumor delineation & have successfully enabled to achieve boost dose of up to 150% of the prescription dose.

Georg et al. in a planning study of ten patients with localized prostate cancer, compared the dose distributions using: volumetric modulated arc therapy (VMAT), scanned proton therapy, scanned carbon-ion therapy, and low dose rate (LDR) and high dose rate (HDR) Brachytherapy treatment of localized prostate cancer [29]. This paper concluded brachytherapy techniques were superior in terms of the bladder wall, rectal wall, and normal tissue sparing. Not just this, the unmatched conformity of brachytherapy also provides the benefit of boosting the resistant tumor to highly lethal dose-something that is a dream with currently practiced EBRT tools.

Carcinoma Cervix: Image-guided brachytherapy has almost replaced point-based brachytherapy planning in carcinoma cervix. The clear benefit of 3D planning in this setting is that there is a potential to optimize the dose to the outlined tumor volume while maintaining acceptable doses to the OARs, thereby reducing the long-term toxicity.

Moreover, the traditional point A dose is a poor surrogate of the HRCTV dose and that MRI-based IGBT significantly improves target coverage and OAR dose [30]. There have been many publications illustrating this effect [31,32,33]. The need to implement 3D imaging for cervix brachytherapy has since been recognized by European, US and United Kingdom (UK) groups such as the European Society of therapeutic radiation oncology (ESTRO), and the Royal College of Radiologists (RCR), who have published recommendations detailing the 3D cervix brachytherapy planning [7,8,36,37,38,39].



Reasons for the Decline of Brachytherapy and Issues to be dealt with

Brachytherapy tends to "fly under the radar" when compared to external beam radiotherapy (EBRT). There have been numerous important, perhaps under-appreciated advances in brachytherapy in the last two decades that still evidently report a decline in Brachytherapy practice. Numerous reasons can be allocated for this behavior.

Resource Limitation: lack of infrastructure & training

Lack of brachytherapy facility in academic institutions & a limited number of trained experts leads to lacunae in the training of young radiation oncologists & physicists in Brachytherapy. Besides, the physician's choice to offer brachytherapy is negatively influenced by limited experience and training, deficient workforce, limited machine & equipment, lack of teamwork, intensive labor, and fear of liable risk. Also, contemporary brachytherapy experts have played their bit in not having disseminated this art to their pupils and perhaps failed to make this field exciting and continuously evolving. As a result, for the current generation IMRT, IGRT, proton beams, chemotherapy & immunotherapy are ruling the roost.

Atomic Energy Regulatory Board (AERB), reported the domination of teletherapy in early 2014 affirming that there are 362 radiotherapy centers in India, equipped with 308 linear accelerators (LA), 238 Telecobalt units, 4 Cyberknife units, 3 Tomotherapy units, 8 Gamma Knife units[40]. Also, there are 232 HDR and 91 LDR brachytherapy units available in the different hospitals across the country. Most of the facilities in the corporate healthcare and upgraded government sectors have upgraded systems for external beam radiotherapy planning, but unfortunately, a survey regarding the up-gradation of brachytherapy facilities and their related details does not exist. Although there are around 323 institutions with brachytherapy machines, more than two-thirds of these, practice only intracavitary treatment for carcinoma cervix[41]. Hence, for most of the beginners pursuing training in radiotherapy, the knowledge on brachytherapy is theoretical, and brachytherapy practical experience, other than intracavitary procedure, is visibly lacking.

The decline in Brachytherapy Directed Clinical Research

Limited clinical trials & reporting of brachytherapy have also led to a major setback in the utilization of this time-tested technique in today's modern era of evidence-based practice. Bismarck C.L. Odei et al have analyzed brachytherapy trials over the year 2000 to 2015[42]. The majority of the clinical trials were phase II (37%), involving interstitial BT (45%). New clinical trials involving radiotherapy of all types showed a significant increase over time ($p < 0.05$), whereas no corresponding increase was seen in BT trials.



Disregard by Various Worldwide Association

Not just the academic institutions & physicians but the various worldwide organizations such as ESTRO, American Society for Therapeutic Radiology and Oncology (ASTRO), and Association of Radiation Oncologists Of India (AROI) have also kept brachytherapy out of the focus area. As an example, of the thirty-five courses listed in the ESTRO calendar for 2012, only three directly address the topic of brachytherapy [43]. The number of conferences and workshops of national and state-level importance that focused on brachytherapy is a handful. In 2013, only two such courses of national importance were organized with not much participation by the oncologists. Out of the 15 teaching courses organized by the 'Indian College of Radiation Oncology (ICRO) in the past eight years for resident doctors, only one was focused on comprehensive brachytherapy. Generally, the interest in learning brachytherapy is gratified by personal pursuance. In the annual conference of the AROI 2012, about nineteen papers of original ongoing work focusing on brachytherapy were presented, out of 198 presentations in all sections.

Strategies to Check the Decline of Brachytherapy

Brachytherapy not only works, but it is also an irreplaceable component of contemporary cancer care. Brachytherapy provides the inherent form of a "conformal treatment or conformal boost." It is a great treatment option that is an absolute requirement of curative therapy in various cancer sites like the cervix, oral cavity, prostate, etc. It has been available for decades and has evolved according to modern radiotherapy tools but the rates of actually using it are dropping. Hence it is high time that we should work together to reignite the blinking blaze to secure this dying art.

Clinicians, physicists, policymakers, therefore, need to spend considerable time and attention to re-explore this technique and take justifiable pride in the outcomes of this technique. The radiation oncology association/bodies should take efforts to join hands, to emphasize and convince the state & central government authorities for the availability of brachytherapy facilities in government institutions and make budgetary provisions and finances available to establish BT facilities where they are not available.

The established brachytherapy centers should augment their facilities for adopting the latest technology-based BT procedures like IGBT. Residents and Physicists should be trained through inter institution exchange programs & by organizing hands-on training by centers having fully developed Brachytherapy set up and the bulk of patients. The academic organizations should create working groups for specialized training and introduce certified courses in Brachytherapy techniques or even a super specialization in Brachytherapy.



In a way to achieve uniformity of brachytherapy application & usage, higher institutes & tertiary cancer care centers should develop site-wise guidelines for dose and fractionation and share data, conduct clinical trials and report/publish their results. Brachytherapy work practiced across the country can be brought into notice by coming up with a journal specifically focusing on brachytherapy. This may encourage people to undertake projects and hypotheses in the field of brachytherapy. Also, Radiation Oncology bodies should give BT its due focus in various activities organized, like conferences, workshops/ continued medical education (CMEs). To ignite the interest of youth, few national & international fellowships should be reserved for brachytherapy. Not just India but the global brachytherapy community should also consider similar steps. All efforts for international collaboration with organizations like ESTRO, ASTRO, Groupe Européen de Curiethérapie (GEC-ESTRO), American brachytherapy Society (ABS), etc. should be made for bilateral exchange programs.

The resurgence of this Age-Old Art

The mark of a good trend is its ability to come back. It is heartening to know that this art is being revitalized again through the effort of the Indian Brachytherapy Society (IBS) established on 16 March 2006, with the main aim of promoting brachytherapy practice, training, and research [44].

The IBS is perpetually working toward installations of more HDR machines with modern applicators & imaging techniques & an updated planning system. The image-guided Brachytherapy is gaining momentum in the Indian scenario. With the efforts of IBS, there has been a surge in the quality and quantity of publications, conferences & CMEs relating to brachytherapy from India in the last few years. One or two universities accredited fellowship courses on the specialty of brachytherapy are ongoing.

The Government of India & the National Medical Council has also been supportive in this regard [45]. The Medical Council has recently increased the number of specialist courses to meet the growing demand. The country is going to have more trained anesthetists and trained radiation oncologists soon. Moreover, an additional number of university-affiliated courses on medical physics and radiotherapy technology has come up in recent time. The government is also funding more for the up-gradation of brachytherapy facilities and procurement of new equipment. With more installations of HDR machines, improved availability of applicators, availability of dedicated operating theaters, anesthesiologists and well-trained radiation oncologists, brachytherapy practices will see a revival in the right direction.

Conclusion

Brachytherapy has a long and illustrious history in the treatment of cancer dating back to the early 20th century. Although its popularity has fluctuated in response to the emergence of newer treatment modalities, yet brachytherapy has persisted over time. Brachytherapy deserves more attention as a



valuable and highly improved technique with unique advantages. We can say brachytherapy is currently going through a period of renaissance and change with more complex techniques involving state-of-the-art imaging and planning. It is the responsibility of all of us "the oncologists" to educate our students, budding radiation oncologists, patients, policymakers & insurers about the critical value of brachytherapy.

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References

1. Roentgen, W. C. "[on a New Kind of Ray (First Report)]." *Munch Med Wochenschr* 101 (1959): 1237-9.
2. Becquerel, J., and J. A. Crowther. "Discovery of Radioactivity." *Nature* 161.4094 (1948): 609.
3. Curie, E. "Marie and Pierre Curie and the Discovery of Radium." *Br J Radiol* 23.271 (1950): 409-12.
4. Tod, Margaret C., and W. J. Meredith. "A Dosage System for Use in the Treatment of Cancer of the Uterine Cervix." *The British Journal of Radiology* 11.132 (1938): 809-24.
5. Paterson, Ralston, and H. M. Parker. "A Dosage System for Interstitial Radium Therapy." *The British Journal of Radiology* 11.124 (1938): 252-66.
6. Meredith WJ. "Radium Dosage : The Manchester System". Edinburgh/London, UK: E&S Livingstone;1967.
7. Haie-Meder, C., et al. "Recommendations from Gynaecological (Gyn) Gec-Estro Working Group (I): Concepts and Terms in 3d Image Based 3d Treatment Planning in Cervix Cancer Brachytherapy with Emphasis on Mri Assessment of Gtv and Ctv." *Radiother Oncol* 74.3 (2005): 235-45
8. Potter, R., et al. "Recommendations from Gynaecological (Gyn) Gec Estro Working Group (II): Concepts and Terms in 3d Image-Based Treatment Planning in Cervix Cancer Brachytherapy-3d Dose Volume Parameters and Aspects of 3d Image-Based Anatomy, Radiation Physics, Radiobiology." *Radiother Oncol* 78.1 (2006): 67-77.
9. Groupe Europ´ een de Curietherapie European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) APBI Trial. Interstitial brachytherapy alone versus external beam radiation therapy after breast-conserving therapy for low-risk invasive carcinoma and low-risk duct carcinoma in-situ (DCIS) of the female breast. 2004. Available from www.aphi.uni-erlangen.de
10. National Surgical Adjuvant Bowel and Breast Project (NSABP). Protocol B-39/RTOG 0413. A randomized phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) for women with stage 0, I, or II breast cancer. 2005. Available from www.nsabp.



pitt.edu/B-39.asp

11. Vicini, F., et al. "Accelerated Partial Breast Irradiation: An Update on Published Level I Evidence." *Brachytherapy* 15.5 (2016): 607-15.
12. Njeh, C. F., M. W. Saunders, and C. M. Langton. "Accelerated Partial Breast Irradiation (Apbi): A Review of Available Techniques." *Radiat Oncol* 5 (2010): 90.
13. Jain, A. K., and R. D. Ennis. "Focal Therapy, Differential Therapy, and Radiation Treatment for Prostate Cancer." *Adv Urol* 2012 (2012): 573193.
14. Kim, Y., et al. "Class Solution in Inverse Planned Hdr Prostate Brachytherapy for Dose Escalation of Dil Defined by Combined Mri/Mrsi." *Radiother Oncol* 88.1 (2008): 148-55.
15. Potter, R., et al. "Clinical Impact of Mri Assisted Dose Volume Adaptation and Dose Escalation in Brachytherapy of Locally Advanced Cervix Cancer." *Radiother Oncol* 83.2 (2007): 148-55.
16. Kirisits, C., et al. "Dose and Volume Parameters for Mri-Based Treatment Planning in Intracavitary Brachytherapy for Cervical Cancer." *Int J Radiat Oncol Biol Phys* 62.3 (2005): 901-11.
17. De Brabandere, M., et al. "Potential of Dose Optimisation in Mri-Based Pdr Brachytherapy of Cervix Carcinoma." *Radiother Oncol* 88.2 (2008): 217-26.
18. Tanderup, K., et al. "From Point a to the Sculpted Pear: Mr Image Guidance Significantly Improves Tumour Dose and Sparing of Organs at Risk in Brachytherapy of Cervical Cancer." *Radiother Oncol* 94.2 (2010): 173-80.
19. Martin, J. M., et al. "The Rise and Fall of Prostate Brachytherapy: Use of Brachytherapy for the Treatment of Localized Prostate Cancer in the National Cancer Data Base." *Cancer* 120.14 (2014): 2114-21.
20. Mahmood, U., et al. "Declining Use of Brachytherapy for the Treatment of Prostate Cancer." *Brachytherapy* 13.2 (2014): 157-62.
21. Yoshioka, Y., et al. "High-Dose-Rate Brachytherapy as Monotherapy for Prostate Cancer: Technique, Rationale and Perspective." *J Contemp Brachytherapy* 6.1 (2014): 91-8.
22. Kishan, A. U., et al. "Radical Prostatectomy, External Beam Radiotherapy, or External Beam Radiotherapy with Brachytherapy Boost and Disease Progression and Mortality in Patients with Gleason Score 9-10 Prostate Cancer." *JAMA* 319.9 (2018): 896-905.
23. Morris, W. J., et al. "Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the Ascende-Rt Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer." *Int J Radiat Oncol Biol Phys* 98.2 (2017): 275-85.
24. Petereit, D. G., et al. "Brachytherapy: Where Has It Gone?" *J Clin Oncol* 33.9 (2015): 980-2.
25. Han, K., et al. "Trends in the Utilization of Brachytherapy in Cervical Cancer in the United States." *Int J Radiat Oncol Biol Phys* 87.1 (2013): 111-9.
26. Gill, B. S., et al. "National Cancer Data Base Analysis of Radiation Therapy Consolidation Modality



for Cervical Cancer: The Impact of New Technological Advancements." *Int J Radiat Oncol Biol Phys* 90.5 (2014): 1083-90.

27. Eifel, P. J., et al. "Patterns of Radiation Therapy Practice for Patients Treated for Intact Cervical Cancer in 2005 to 2007: A Quality Research in Radiation Oncology Study." *Int J Radiat Oncol Biol Phys* 89.2 (2014): 249-56.

28. Banerjee, S., U. Mahantshetty, and S. Shrivastava. "Brachytherapy in India - a Long Road Ahead." *J Contemp Brachytherapy* 6.3 (2014): 331-5.

29. Georg, D., et al. "Dosimetric Considerations to Determine the Optimal Technique for Localized Prostate Cancer among External Photon, Proton, or Carbon-Ion Therapy and High-Dose-Rate or Low-Dose-Rate Brachytherapy." *Int J Radiat Oncol Biol Phys* 88.3 (2014): 715-22.

30. Tanderup, K., et al. "From Point a to the Sculpted Pear: Mr Image Guidance Significantly Improves Tumour Dose and Sparing of Organs at Risk in Brachytherapy of Cervical Cancer." *Radiother Oncol* 94.2 (2010): 173-80.

31. Lindegaard, J. C., et al. "Mri-Guided Adaptive Radiotherapy in Locally Advanced Cervical Cancer from a Nordic Perspective." *Acta Oncol* 52.7 (2013): 1510-9.

32. Lindegaard, J. C., et al. "Mri-Guided 3d Optimization Significantly Improves Dvh Parameters of Pulsed-Dose-Rate Brachytherapy in Locally Advanced Cervical Cancer." *Int J Radiat Oncol Biol Phys* 71.3 (2008): 756-64.

33. De Brabandere, M., et al. "Potential of Dose Optimisation in Mri-Based Pdr Brachytherapy of Cervix Carcinoma." *Radiother Oncol* 88.2 (2008): 217-26.

34. Viswanathan, A. N., et al. "American Brachytherapy Society Consensus Guidelines for Locally Advanced Carcinoma of the Cervix. Part I: General Principles." *Brachytherapy* 11.1 (2012): 33-46.

35. Viswanathan, A. N., et al. "American Brachytherapy Society Consensus Guidelines for Locally Advanced Carcinoma of the Cervix. Part II: High-Dose-Rate Brachytherapy." *Brachytherapy* 11.1 (2012): 47-52.

36. Tan, L. T. "Implementation of Image-Guided Brachytherapy for Cervix Cancer in the Uk: Progress Update." *Clin Oncol (R Coll Radiol)* 23.10 (2011): 681-4.

37. Viswanathan, A. N., et al. "Computed Tomography Versus Magnetic Resonance Imaging-Based Contouring in Cervical Cancer Brachytherapy: Results of a Prospective Trial and Preliminary Guidelines for Standardized Contours." *Int J Radiat Oncol Biol Phys* 68.2 (2007): 491-8.

38. Potter, R., et al. "Image-Guided Adaptive Brachytherapy for Cervix Carcinoma." *Clin Oncol (R Coll Radiol)* 20.6 (2008): 426-32.

39. Dimopoulos, J. C., et al. "Dose-Volume Histogram Parameters and Local Tumor Control in Magnetic Resonance Image-Guided Cervical Cancer Brachytherapy." *Int J Radiat Oncol Biol Phys* 75.1 (2009): 56-63.

40. Atomic Energy Regulatory Board. <http://www.aerb.gov.in/AERBPortal/eLORA.htm>



41. Deshpande, D. D. "Will Mr Image-Guided Brachytherapy Be a Standard of Care for Cervical Cancer in Future? An Indian Perspective." *J Med Phys* 37.1 (2012): 1-3.
42. Odei, B.C., et al. "A comprehensive Analysis of Brachytherapy Clinical Trails over the past 15 years." *Brachytherapy* 15.6(2016): 679-86.
43. Available from: <http://www.estro-education.org/courses/Pages/2012%20Courses.aspx>.
44. Indian Brachytherapy Society. <http://www.indianbrachytherapy.com>.
45. Goss, P. E., et al. "Challenges to Effective Cancer Control in China, India, and Russia." *Lancet Oncol* 15.5 (2014): 489-538.

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