Chapter 12

Advanced Treatment Techniques In Radiotherapy

Ayse Gulbin Kavak[1]

Abstract

Radiotherapy is used to destroy cancer cells or control their growth. The main purpose of radiotherapy is to protect healthy organs while destroying the tumor. Ionization radiations such as x-rays, gamma rays and proton particles are used in radiation therapy. Nowadays, advanced treatment techniques are used when applying radiotherapy to cancer patients. Advanced treatment techniques have been developed to target cancer cells and protect healthy tissues, increase the effectiveness of radiotherapy and minimize side effects. Treatment techniques applied in radiotherapy largely depend on the development of technology. With the developments in computer technology, imaging methods have improved, and parallel to these, there have been developments in radiotherapy techniques. There are many advanced treatment techniques used in radiation therapy. The main ones are intensity-modulated radiation therapy, image-guided radiation therapy, stereotactic radiosurgery and stereotactic body radiation therapy, adaptive radiotherapy, brachytherapy, hypofractionation and proton therapy. Intensity modulated radiation therapy (IMRT) is a treatment technique that uses different beams of light to the targeted volume, destroying cancer cells while sparing surrounding tissues. Image guided radiation therapy (IGRT) uses real-time image guidance during treatment. Patient position and tumor movements are observed so that the target can be treated more accurately. Stereotactic Radiosurgery and Stereotactic Body Radiotherapy are basically based on treating small lesions by focusing on them with very high doses of radiation. Adaptive radiotherapy is a radiotherapy technique that takes into account the patient's anatomical and physiological changes during cancer treatment. This technique makes it possible to update the radiotherapy plan in response to changes in the patient's body and to provide a treatment that targets the radiation dose more precisely. Brachytherapy is a treatment technique that

1 Assistant Professor, Gaziantep University, Medical Faculty, Radiation Oncology Department, kavakgulbin@gmail.com, https://orcid.org/0000-0003-1995-1642

https://doi.org/10.58830/ozgur.pub305.c1257

involves placing radioactive sources directly or very closely into or near cancer cells. Hypofractionation involves giving higher doses to the patient in a shorter period of time compared to conventional radiotherapy fractionation. Proton therapy is a treatment that targets cancer cells using proton-charged particles instead of x-rays or gamma rays. Advanced treatment techniques in radiotherapy offer more options and higher success rates in cancer treatment. However, the type of cancer for each disease differs from each other, so it is very important to determine the most appropriate treatment approach for the patient.

Radiotherapy

Radiotherapy is a medical procedure used in the treatment of cancer. The goal of radiotherapy is to use high-energy radiation to eradicate cancer cells or control their growth. While targeting cancer cells for destruction, radiotherapy aims to minimize damage to the surrounding healthy tissues. The objectives of radiotherapy can be listed as follows: to destroy cancer cells or control their growth, reduce the tumor size, alleviate or eliminate cancer symptoms (Jaffray et al., 2007)

Radiation therapy is divided into external radiotherapy and internal radiotherapy:

In external radiotherapy, high-energy X-rays are applied from the outside to the tumoral area. High-energy radiation beams are generated by a machine for external radiotherapy and directed externally at the patient's body to target and treat cancerous cells or tumors (Jaffray et al., 2007).

In internal radiotherapy which is called brachytherapy , the radiation source is placed directly inside the tumor or body cavities (Ragde, 2004).

The process of radiotherapy starts with imaging. Firstly, a Computed Tomography (CT) images of the patient are obtained in DICOM format. The CT image is then transferred to the treatment planning system. The images transferred to the treatment planning system are fused with magnetic resonance imaging (MRI) and/or positron emission tomography (PET) images to contour the target volume. Precise planning is essential for the effectiveness and safety of radiotherapy. In treatment planning, the aim is to deliver the desired dose to the tumor while protecting the surrounding healthy organs. The radiation dose and treatment duration to be administered to the patient are determined based on the type of cancer and the stage of the disease. Patient treatment planning in radiotherapy is done by selecting the appropriate device, energy, and treatment techniques for the tumor. The most current treatment techniques applied to patients are described in detail below (Schneider et al., 1996).

1. Intensity Modulated Radiation Therapy (IMRT)

Intensity-Modulated Radiation Therapy (IMRT) is one of the significant developments in the field of radiation oncology. IMRT aims to deliver radiation to the tumor with precision, minimizing damage to the surrounding healthy tissues. One of the primary goals of radiation therapy is to minimize the damage to healthy tissues while delivering a therapeutic dose of radiation to the tumor. IMRT represents a paradigm shift in radiation oncology treatment, allowing different dose distributions to different target volumes. The origins of IMRT can be traced back to three-dimensional conformal radiation therapy, which aimed to improve the accuracy of radiation delivery (Ezzell et al., 2003). While the concept of modulating radiation intensity was proposed in the 1980s, it was the development of computer technology and advanced treatment planning systems that made clinical IMRT possible. The first clinical IMRT treatments began in the early 1990s and marked a significant milestone in radiation therapy (Jaffray et al., 2007).

IMRT is based on inverse treatment planning, where the desired dose distribution is determined, and the treatment planning system calculates the optimal intensity pattern for each beam to achieve this distribution. This approach is in contrast to conventional radiation therapy, which relies on forward planning (Jaffray et al., 2007).

IMRT divides each treatment field into multiple beams, each with different intensities. By modulating these beams according to intensity, an optimal dose distribution is achieved that conforms to the shape of the tumor. The accuracy of the dose delivered to the patient is just as important as the planning of IMRT. When planning in IMRT, a reverse optimization plan is made by entering the objectives and priority values for the target volume and critical organs into the system. Additionally, an IMRT plan can be made by using the multicriteria optimization algorithm found in some treatment planning systems. (Kavak et al. 2022). Multileaf collimators (MLCs) are lead plates composed of a series of thin leaves located inside the treatment device head. IMRT heavily relies on MLCs, which can shape the radiation field during treatment. This technology allows precise and rapid modulation of radiation intensity, enhancing dose conformity. With the development of MLCs, Volumetric Modulated Arc Therapy (VMAT) has also become applicable. It is a more advanced treatment technique than IMRT. VMAT treatments can be delivered accurately and effectively with single or multiple arcs. In Volumetric Modulated Arc Therapy, unlike IMRT, VMAT delivery is more complex than IMRT because the gantry rotation speed, dose rate and MLC shape are constantly changing at the same time. The primary advantage of Volumetric Modulated Arc Therapy is that it can treat the patient much faster than fixed gantry IMRT. (Surucu et al., 2012). Before starting IMRT, a patient-specific quality control test is required. Once these quality control tests meet the eligibility criteria, IMRT or VMAT treatment can be approved. IMRT is generally applied to cancer types such as head and neck cancer, prostate cancer, and brain tumors, among others. IMRT is one of the methods that maximize therapeutic effect in cancer treatment (Jaffray et al., 2007).

2. Image-Guided Radiation Therapy

Image-Guided Radiation Therapy (IGRT) represents a revolutionary approach in the implementation of radiation therapy, offering a dynamic and adaptable approach to cancer treatment. IGRT is a significant advancement in the field of radiation oncology and plays a central role in providing precise and personalized radiation therapy while minimizing the impact on healthy tissues (Xing et al., 2006).

The roots of IGRT may date back to the 1990s when it emerged as an extension of traditional radiation therapy. The development of IGRT has progressed in parallel with advances in medical imaging that enable the integration of real-time imaging and treatment delivery (Simpson et al., 2010).

The fundamental principle of IGRT is precise target localization. IGRT ensures that the tumor or target volume is accurately positioned and monitored in real-time during radiation delivery, not only during the treatment planning phase. This allows for adjustments to be made based on the target's position, shape, and size at any given moment. IGRT enables adaptable treatment planning that can accommodate changes in the patient's anatomy or tumor response during treatment, making it particularly valuable in managing anatomical changes caused by factors such as weight loss, tumor regression, or organ motion (Bissonnette et al., 2012).

With technological advancements, IGRT makes use of various imaging techniques such as cone-beam computed tomography (CBCT), positron emission tomography (PET), magnetic resonance imaging (MRI), and ultrasound (Simpson et al., 2010).

IGRT has a wide range of applications in clinical practice for various cancer types, including prostate cancer, lung cancer, head and neck cancer, gynecological cancers, brain tumors, and pediatric tumors (Perkins et al., 2006). The ability to precisely target tumors in IGRT enhances the effectiveness of this treatment method. Ensuring the accuracy and safety of IGRT is crucial. Regular equipment calibration, image registration, and staff training are essential. Quality assurance measures are also important for minimizing errors and ensuring patient safety. IGRT enables personalized treatment plans, advanced patient comfort, and convenience (Bissonnette et al., 2012).

3. Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT)

Stereotactic radiosurgery (SRS) is a radiation therapy used to treat functional abnormalities and small tumors in the brain. In SRS treatment, a higher dose of radiation is applied in fewer fractions compared to conventional treatment, which helps better preserve healthy tissue (Combs et al., 2005). When used to treat body tumors, it is referred to as stereotactic body radiation therapy (SBRT) (Okunieff et al., 2006). SRS and SBRT can be considered groundbreaking treatment methods in radiation oncology. These concepts emerged in the early 20th century with the development of stereotactic frames for brain surgery (Combs et al., 2005). However, their application in radiation therapy began in the 1980s and has rapidly advanced since then. Technological advancements and clinical evidence have facilitated their adoption.

The main principles of SRS and SBRT are high precision and conformity (Schefter et al., 2005). They deliver high doses of radiation to the target with sub-millimeter accuracy while minimizing exposure to surrounding healthy tissues. This is achieved through the best targeting and immobilization techniques of the tumor. In SRS, a typical treatment involves delivering a single high dose in a single session, while the SBRT concept allows for the treatment of larger and more irregularly shaped tumors by extending it to several or more fractions (Vergalasova et al., 2019).

SRS and SBRT heavily rely on advanced imaging methods such as Cone Beam Computed Tomography (CBCT), Magnetic Resonance Imaging (MRI), and Positron Emission Tomography (PET) for real-time guidance in treatment planning and delivery.

SRS and SBRT are applied to conditions such as brain metastases, primary brain tumors, lung cancer, spine and bone metastases, liver tumors, and prostate cancers. Precise dose optimization algorithms are used for SRS and SBRT to ensure the target receives a therapeutic dose while minimizing normal tissue toxicity (Samlowski et al., 2007). Robust quality assurance measures, including device calibration, image registration, and personnel training, are necessary to guarantee the safety and accuracy of SRS and

SBRT treatments. Studies have shown high local control rates, reduced side effects, improved quality of life, and increased survival rates with SRS and SBRT. With ongoing technological advancements and expanding clinical indications, SRS and SBRT will continue to play an increasingly prominent role in modern oncology (Okunieff et al., 2006).

4. Adaptive Radiation Therapy

In the constantly evolving field of radiation oncology, Adaptive Radiation Therapy (ART) has emerged as a significant advancement. ART represents a dynamic, patient-centric approach to cancer treatment that harnesses the power of precise medicine and technology to minimize potential harm while maximizing therapeutic efficacy. It is an innovative approach to delivering radiation therapy to cancer patients. Traditional radiation therapy methods often rely on a one-dimensional approach where treatment plans are designed based on initial imaging and clinical evaluations (Sonke et al., 2019). However, tumors are not static and can change in size, shape, and location during the course of treatment. This variability poses a significant challenge in ensuring that the intended radiation therapy reaches its target while sparing healthy tissues (Sonke et al., 2019).

ART is designed to address this challenge by adapting the radiation treatment plan to these changes. It integrates advanced imaging techniques like Magnetic Resonance Imaging (MRI) or Positron Emission Tomography (PET) into the radiation therapy process. In ART, continuous monitoring of the tumor's response to treatment and real-time adjustments when needed are essential. ART often utilizes intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT) to further customize the radiation dose distribution (Aydogan et al., 2011). ART's versatility allows for the implementation of various plans in cancer treatment (Castelli et al., 2018).

One of the key applications of ART is monitoring tumor regression and adapting to it. As radiation therapy progresses, tumors can shrink or change shape. By acquiring new patient images, treatment plans are adjusted to ensure that the tumor remains within the radiation field, allowing the therapeutic dose to be delivered to the tumor while minimizing damage to surrounding healthy tissues (Roth et al., 2020). Conversely, for tumors exhibiting growth or changes in size, ART is necessary to continue treatment. Detecting these changes early allows for the readjustment of the treatment plan to encompass the tumor volume and prevent low doses within the tumor.

Another critical aspect of ART is its ability to protect at-risk organs. Continuous monitoring allows for adjustments to the treatment plan when critical structures near the tumor are at risk of receiving excessive radiation. This feature improves the protection of critical organs like the spinal cord, brainstem, heart, and lungs when they are in close proximity to the tumor (Sonke et al., 2019).

ART also helps optimize fractionation schedules. In some cases, treatment may need adjustments based on the tumor's response. For instance, if a tumor responds well to radiation therapy, the treatment plan can be adjusted to shorten the treatment duration, thereby reducing the patient's overall radiation exposure. ART is one way to minimize the risk of complications arising from re-irradiation for patients who have previously undergone radiation therapy and require retreatment. By avoiding previously irradiated areas, the treatment plan can be precisely adapted to enhance the feasibility of re-treatment (Keall et al., n.d.).

Due to the dynamic nature of ART, it provides increased treatment accuracy and effectiveness by aligning with changes in tumor position and size. It minimizes exposure of healthy tissues to radiation, thereby reducing treatment-related side effects and improving the patient's quality of life. The dynamic nature of ART can be attributed to better tumor control and increased likelihood of successful treatment outcomes (Keall et al., n.d.).

While ART represents a revolutionary approach, it comes with its challenges and considerations. Implementing ART requires a skilled technical team and technical expertise. The application of ART relies on advanced imaging and specialized treatment planning techniques. Continuous monitoring and plan adaptation can be time-consuming in terms of both time and equipment. ART is not suitable for every patient and cancer type, as its application depends on individual circumstances and the feasibility of real-time adaptation. To effectively harness the full potential of ART, ongoing research and education are essential. As technology continues to advance, ART will become even more precise and widely accessible. Artificial intelligence and machine learning are likely to play a significant role in automating and facilitating the adaptation process. The future of ART holds promises for further improving cancer treatment outcomes, reducing side effects, and enhancing the patient experience.

In conclusion, ART represents a monumental shift in the approach to cancer treatment. By acknowledging the dynamic nature of tumors, it adapts treatment plans accordingly. With numerous benefits such as increased precision, reduced side effects, and improved tumor control, ART is at the forefront of modern radiation oncology (Keall et al., n.d.).

5. BRACHYTHERAPY

Brachytherapy, commonly referred to as "internal radiation therapy," is a highly effective and localized approach in the treatment of various cancer types. This treatment technique involves the direct placement of sealed radioactive sources into or near the tumor, allowing for precise radiation delivery while minimizing exposure to surrounding healthy tissues. Brachytherapy has a rich history that spans over a century, with its roots tracing back to the pioneering work of early physicists like Pierre and Marie Curie, who discovered radioactive elements radium and polonium (Chargari et al., 2019). These discoveries laid the foundation for the development of brachytherapy techniques, with the first clinical applications reported in the early 20th century. Since then, significant advancements have been made in brachytherapy (Chargari et al., 2019).

Brachytherapy is a treatment technique that utilizes various radioactive sources. The selection of appropriate sources depends on the type, size, and location of the tumor. Precise dosimetry is crucial in brachytherapy to ensure the safe and effective delivery of radiation. The application of brachytherapy involves special equipment and procedures, including applicators, catheters, and after loaders (Nag et al., 2000).

Brachytherapy is categorized as interstitial, intracavitary, and surface brachytherapy. Interstitial brachytherapy involves the direct placement of radioactive sources into or near the tumor. Examples include prostate implants and breast cancer. Intracavitary brachytherapy entails the placement of radioactive sources into natural body cavities such as the cervix or esophagus. Surface brachytherapy is used to treat skin cancers and other superficial lesions (Ragde, 2004).

Brachytherapy plays a significant role in the treatment of gynecological cancers, including cervical, uterine, and vaginal cancers. It can also be considered as an alternative method for delivering radiation to the entire breast in breast cancer patients. Over the years, brachytherapy has evolved into a precise, effective, and well-tolerated cancer treatment method. Ongoing research and technological innovations continue to offer hope, promising better outcomes and quality of life for cancer patients. The potential for brachytherapy to play a more important role in cancer treatment in the future is both exciting and promising (Chargari et al., 2019).

6. Hypofractionation

Radiation therapy has become the cornerstone of cancer treatment, applied before or after surgery, in conjunction with chemotherapy. Radiation therapy provides an effective tool to target and destroy cancer cells. Conventional radiation therapy programs typically involve giving conventional doses of radiation therapy 5 days per week. However, the scope of radiation therapy is evolving and a new approach called hypofractionation is gaining importance (Jones et al., 2000).

Hypofractionation is a departure from traditional radiation therapy techniques. Hypofractionation involves giving larger doses of radiation in fewer treatment sessions, rather than giving smaller doses of radiation over a long period of time. This approach offers several advantages for both patients. The most important of these is the shortening of treatment time in terms of patient comfort. With traditional radiation therapy, patients often need to visit the treatment center for several weeks; This can be financially and spiritually difficult and disrupt their daily lives (Jones et al., 2000). Hypofractionation, on the other hand, allows for a significantly shorter treatment period. Patients can complete their treatment within a few days or weeks, reducing the time and effort required for travel and treatment. Shorter treatment programs mean fewer clinic visits and reduce the financial burden on both patients and healthcare systems (Hunter et al., 2018). Hypofractionation is therefore critical in the context of rising healthcare costs and limited resources. Hypofractionation not only reduces the number of treatment sessions but also eases transportation difficulties for patients (Hunter et al., 2018). This is especially helpful for people who live far from the treatment center. The intensified treatment program of hypofractionation generally results in fewer side effects and a more comfortable experience for patients. This can be said to have a positive impact on the overall quality of life during and after radiation therapy (Jones et al., 2000).

Hypofractionation is a versatile technique that can be applied to various types of cancer, including breast, prostate, lung and brain cancer. Its effectiveness is supported by extensive clinical research showing that larger radiation doses delivered in fewer fractions can provide the same level of tumor control as conventional fractionation (Hegemann et al., 2014).

Hypofractionation has begun to be used very frequently in breast cancer treatment. Clinical experience has shown that administering higher doses in fewer fractions after breast-conserving surgery is not only safe but can also provide equivalent or even better results compared to conventional radiation therapy (Hickey et al., 2016).

Hypofractionated radiation therapy has become widely used in the treatment of prostate cancer. It offers a balance between effective cancer control and patient convenience. Research shows that this approach can be as effective as traditional radiation therapy, with the advantage of shorter treatment time (Hegemann et al., 2014).

Hypofractionation is advantageous for lung and brain cancer patients. These cancers are often found in areas close to critical organs. Delivering higher radiation doses in fewer sessions provides better tumor control and minimizes damage to surrounding healthy tissues (Hegemann et al., 2014).

Although hypofractionation has its benefits, it also has its challenges and considerations. Careful patient selection, advanced imaging techniques, and precise treatment planning are crucial to maximize the benefits of this approach while minimizing the risk of side effects (Haffty, 2010).

In spite of hypofractionation is an exciting development in the field of radiation therapy, offering patients a shorter and more cost-effective treatment option, it should be applied with caution due to the high dose delivered. As technology continues to advance, radiation therapy will become more precise and personalized, leading to better outcomes for cancer patients. Hypofractionation represents a significant advance that has the potential to improve the lives of countless cancer patients worldwide. In the future, hypofractionation techniques will continue to advance and improve (Jones et al., 2000).

7. Proton Therapy

In recent years, advances in medical technology have revolutionized the field of cancer treatment. The most important of these is proton therapy, a cutting-edge method that offers significant advantages over traditional radiation therapy. Proton therapy uses protons, positively charged particles, to target cancer cells with extraordinary precision (Bussière & Adams, 2003).

Proton therapy is a form of radiation therapy that uses charged particles, protons, to treat cancer. Unlike traditional X-ray or photon therapy, which uses high-energy photons, proton therapy uses protons that can be precisely controlled in terms of their speed and energy. This makes it possible to deliver the radiation dose more accurately, minimizing damage to healthy tissues and vital organs surrounding the tumor (Sánchez-Parcerisa et al., 2014).

The Particle Acceleration process begins with a particle accelerator, which produces protons and accelerates them to the desired energy level. Protons are then directed into the treatment chamber through an array of magnets.

One of the most important advantages of proton therapy is the precise control of the energy of protons. This allows protons to adjust the range and depth of penetration into the body, allowing protons to deliver the maximum radiation dose precisely into the tumor, sparing healthy tissues (Bussière & Adams, 2003).

Before treatment begins, detailed imaging such as CT scans and MRIs are used to create a treatment plan that outlines the exact location of the tumor and the path the protons will take. The medical team creates a treatment plan to configure the accelerator and magnets for each patient's unique situation. After the treatment plan is created, protons are directed to the tumor in a highly controlled manner. This minimizes radiation exposure to surrounding healthy tissue and critical structures.

Proton therapy has shown promising results in various types of cancer, especially in cases where preserving surrounding healthy tissue is crucial. Some notable applications include:

Pediatric Cancer: Children's developing bodies are very pediatrically sensitive to radiation, making proton therapy an excellent option for cancer cases. It minimizes the risk of long-term side effects and secondary cancer (Roth et al., 2020).

Brain Tumors: Proton therapy is highly effective in treating brain tumors because it allows precise targeting near critical structures such as the optic nerves and brainstem (Skaarup et al., 2021).

Prostate Cancer: Proton therapy has become a popular choice for treating prostate cancer due to its ability to protect the rectum and bladder from radiation exposure (Skaarup et al., 2021).

Head and Neck Cancers: Cancers in the head and neck area can be difficult to treat without damaging important structures such as salivary glands and vocal cords. Proton therapy reduces secondary damage. It reduces the side effects of Proton Therapy. Proton therapy minimizes radiation exposure to healthy tissues, often leading to reduced short-term side effects such as nausea and skin irritation. Proton therapy is associated with a reduced risk of long-term complications and improves patients' quality of life after treatment. The accuracy of proton therapy results in a higher dose of radiation being delivered to the tumor, potentially increasing the effectiveness of the treatment. It may reduce the risk of secondary cancers caused by radiation therapy because healthy tissues are exposed to less radiation (Skaarup et al., 2021).

Proton therapy is a remarkable advance in cancer treatment; it offers better sensitivity and less collateral damage compared to traditional radiation therapy. As technology continues to advance, it holds great promise for a broader range of cancer types and patients. The field of proton therapy is still evolving, and ongoing research and development are expected to further advance this innovative approach to cancer care (Vanderwaeren et al., 2021).

8. Radiomics and Artificial Intelligence (AI) in Radiation Therapy

Radiation therapy plays a crucial role in treating cancer patients, allowing precise targeting of tumors while sparing healthy tissues. The integration of radiomics and artificial intelligence (AI) into radiation therapy has led to a transformative paradigm shift in the field. Radiomics is an emerging field in medical imaging that focuses on the extraction of high-dimensional data from radiological images (Lohmann et al., 2020). These data include not only standard anatomical information but also textural and quantitative features that describe the heterogeneity, shape, and spatial distribution of tumor and healthy tissues. Radiomics can provide a basis for more precise treatment planning and response assessment by extracting valuable information normally imperceptible to the human eye. The role of radiomics in Radiation Therapy is important. Radiomics offers the ability to predict a tumor's response to radiation therapy. By analyzing pretreatment imaging data, radiomics features can provide insights into tumor behavior and help radiation oncologists tailor treatment plans to the specific characteristics of the tumor. Radiomics during and after radiation therapy can help evaluate response to treatment. By measuring changes in tumor tissue and shape over time, radiomics analysis can provide early indicators of the effectiveness of treatment or the need for treatment modification (Arimura et al., 2019).

Artificial intelligence, especially machine learning and deep learning, is beginning to become an important component of radiation therapy. Artificial intelligence algorithms can aid in treatment planning, decision-making, and real-time adaptation by processing and analyzing large amounts of radiomics data (Fu et al., 2022). AI algorithms can optimize radiation treatment plans by considering radiomics data to determine ideal beam angles, dose distribution, and fractionation schedules. This leads to more effective tumor control and reduced damage to surrounding healthy tissues. The automation of contouring and segmentation tasks in radiation therapy has been greatly improved thanks to artificial intelligence. Significantly reduces the time and variability associated with manual identification of structures, increasing efficiency and consistency in the treatment planning process. AI-powered adaptive radiation therapy allows real-time adaptation of treatment plans based on daily imaging. This ensures that treatment remains accurate even if there are anatomical changes in the patient between sessions (Lohmann et al., 2020).

Although radiomics and artificial intelligence have great potential in radiation therapy, they present some challenges. In artificial intelligence, data quality and standardization are important. High-quality and standardized imaging data is required for radiomics and AI analyses. Variability in imaging protocols and equipment can pose challenges to accurate and reproducible results. Translating radiomics and AI tools from research to clinical application requires rigorous validation and integration with existing treatment protocols. Patient data privacy, algorithm transparency, and regulatory approvals are critical issues that must be addressed as AI technologies are incorporated into clinical practice (Fu et al., 2022).

The synergy between radiomics and artificial intelligence in radiation therapy is an evolving field with ongoing research and development. In the future, AI may be able to provide personalized treatment planning based on radiomics and genomic data. It can perform patient-specific treatment adaptation using real-time imaging and artificial intelligence. It may integrate with other methods, such as genomics, for a comprehensive understanding of cancer behavior (Arabi & Zaidi, 2020).

Ultimately, radiomics and artificial intelligence have the potential to revolutionize radiation therapy by providing more precise and personalized treatment options. As technology continues to advance and research progresses, the integration of these tools into clinical practice will improve patient outcomes and reinforce the essential role of radiation therapy in cancer treatment (Huynh et al., 2020).

These advanced treatment techniques in radiotherapy aim to optimize the balance between tumor control and healthy tissue preservation, reducing side effects of treatment and improving overall treatment outcomes. The choice of technique depends on the specific cancer type, stage, location and patient characteristics and is determined by a multidisciplinary approach including radiation oncologists, medical physicists and dosimetrists (Lohmann et al., 2020).

References

Arabi, H., & Zaidi, H. (2020). Applications of artificial intelligence and deep learning in molecular imaging and radiotherapy. In *European Journal of Hybrid Imaging* (Vol. 4, Issue 1). https://doi.org/10.1186/s41824-020-00086-8

Arimura, H., Soufi, M., Kamezawa, H., Ninomiya, K., & Yamada, M. (2019). Radiomics with artificial intelligence for precision medicine in radiation therapy. *Journal of Radiation Research*, *60*(1), 150–157. https://doi.org/10.1093/jrr/rry077

Aydogan, B., Yeginer, M., Kavak, G. O., Fan, J., Radosevich, J. A., & Gwe-Ya, K. (2011). Total marrow irradiation with RapidArc volumetric arc therapy. *International Journal of Radiation Oncology Biology Physics*, *81*(2), 592–599. https://doi.org/10.1016/j.ijrobp.2010.11.035

Bissonnette, J. P., Balter, P. A., Dong, L., Langen, K. M., Lovelock, D. M., Miften, M., Moseley, D. J., Pouliot, J., Sonke, J. J., & Yoo, S. (2012). Quality assurance for image-guided radiation therapy utilizing CT-based technologies: A report of the AAPM TG-179. *Medical Physics*, *39*(4), 1946–1963. https://doi.org/10.1118/1.3690466

Bussière, M. R., & Adams, J. A. (2003). Treatment Planning for Conformal Proton Radiation Therapy. *Technology in Cancer Research and Treatment*, *2*(5), 389–399. https://doi.org/10.1177/153303460300200504

Castelli, J., Simon, A., Lafond, C., Perichon, N., Rigaud, B., Chajon, E., De Bari, B., Ozsahin, M., Bourhis, J., & de Crevoisier, R. (2018). Adaptive radiotherapy for head and neck cancer. In *Acta Oncologica* (Vol. 57, Issue 10, pp. 1284–1292). https://doi.org/10.1080/0284186X.2018.1505053

Chargari, C., Deutsch, E., Blanchard, P., Gouy, S., Martelli, H., Guérin, F., Dumas, I., Bossi, A., Morice, P., Viswanathan, A. N., & Haie-Meder, C. (2019). Brachytherapy: An overview for clinicians. *CA: A Cancer Journal for Clinicians*, *69*(5), 386–401. https://doi.org/10.3322/caac.21578

Combs, S. E., Widmer, V., Thilmann, C., Hof, H., Debus, J., & Schulz-Ertner, D. (2005). Stereotactic radiosurgery (SRS): Treatment option for recurrent glioblastoma multiforme (GBM). *Cancer*, *104*(10), 2168–2173. https://doi.org/10.1002/cncr.21429

Ezzell, G. A., Galvin, J. M., Low, D., Palta, J. R., Rosen, I., Sharpe, M. B., Xia, P., Xiao, Y., Xing, L., & Yu, C. X. (2003). Guidance document on delivery, treatment planning, and clinical implementation of IMRT: Report of the IMRT subcommittee of the AAPM radiation therapy committee. *Medical Physics*, *30*(8), 2089–2115. https://doi.org/10.1118/1.1591194

Fu, Y., Zhang, H., Morris, E. D., Glide-Hurst, C. K., Pai, S., Traverso, A., Wee, L., Hadzic, I., Lonne, P. I., Shen, C., Liu, T., & Yang, X. (2022). Artificial Intelligence in Radiation Therapy. *IEEE Transactions on Radiati-*

on and Plasma Medical Sciences, *6*(2), 158–181. https://doi.org/10.1109/TRPMS.2021.3107454

Haffty, B. G. (2010). Long-term results of hypofractionated radiation therapy for breast cancer. In *Breast Diseases* (Vol. 21, Issue 3, pp. 267–268). https://doi.org/10.1016/S1043-321X(10)79594-1

Hegemann, N. S., Guckenberger, M., Belka, C., Ganswindt, U., Manapov, F., & Li, M. (2014). Hypofractionated radiotherapy for prostate cancer. In *Radiation Oncology* (Vol. 9, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13014-014-0275-6

Hickey, B. E., James, M. L., Lehman, M., Hider, P. N., Jeffery, M., Francis, D. P., & See, A. M. (2016). Hypofractionated radiation therapy for early breast cancer. *Cochrane Database of Systematic Reviews*, *2017*(9). https://doi.org/10.1002/14651858.cd003860.pub4

Hunter, D., Mauldon, E., & Anderson, N. (2018). Cost-containment in hypofractionated radiation therapy: a literature review. In *Journal of Medical Radiation Sciences* (Vol. 65, Issue 2, pp. 148–157). John Wiley and Sons Ltd. https://doi.org/10.1002/jmrs.273

Huynh, E., Hosny, A., Guthier, C., Bitterman, D. S., Petit, S. F., Haas-Kogan, D. A., Kann, B., Aerts, H. J. W. L., & Mak, R. H. (2020). Artificial intelligence in radiation oncology. In *Nature Reviews Clinical Oncology* (Vol. 17, Issue 12, pp. 771–781). https://doi.org/10.1038/s41571-020-0417-8

Jaffray, D., Kupelian, P., Djemil, T., & Macklis, R. M. (2007). Review of image-guided radiation therapy. In *Expert Review of Anticancer Therapy* (Vol. 7, Issue 1, pp. 89–103). Future Drugs Ltd. https://doi.org/10.1586/14737140.7.1.89

Jones, B., Dale, R. G., Finst, P., & Khaksar, S. J. (2000). Biological equivalent dose assessment of the consequences of hypofractionated radiotherapy. *International Journal of Radiation Oncology Biology Physics*, *47*(5), 1379–1384. https://doi.org/10.1016/S0360-3016(00)00571-X

Kavak, A. G., Coşkun, H., & Demiryürek, A. T. (2022). Lokalize prostat kanserli hastalarda yoğunluk ayarlı radyoterapi (IMRT) tekniği kullanılarak standart optimizasyon yöntemi ile çok kriterli optimizasyon (MCO) yönteminin karşılaştırılması. European Journal of Science and Technology, 38, 16–23. https://doi.org/10.31590/ejosat.1078027

Keall, P., Poulsen, P., oncology, J. B.-S. in radiation, & 2019, undefined. (n.d.). See, think, and act: real-time adaptive radiotherapy. *Elsevier*. Retrieved October 15, 2023, from https://www.sciencedirect.com/science/article/pii/S1053429619300141

Lohmann, P., Bousabarah, K., Hoevels, M., & Treuer, H. (2020). Radiomics in radiation oncology—basics, methods, and limitations. In *Strahlentherapie und Onkologie* (Vol. 196, Issue 10, pp. 848–855). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s00066-020-01663-3

Nag, S., Erickson, B., Thomadsen, B., Orton, C., Demanes, J. D., & Petereit, D. (2000). The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. *International Journal of Radiation Oncology Biology Physics*, *48*(1), 201–211. https://doi.org/10.1016/S0360-3016(00)00497-1

Okunieff, P., Petersen, A. L., Philip, A., Milano, M. T., Katz, A. W., Boros, L., & Schell, M. C. (2006). Stereotactic Body Radiation Therapy (SBRT) for lung metastases. *Acta Oncologica*, *45*(7), 808–817. https://doi.org/10.1080/02841860600908954

Perkins, C. L., Fox, T., Elder, E., Kooby, D. A., Staley, C. A., & Landry, J. (2006). Image-guided radiation therapy (IGRT) in gastrointestinal tumors. *Journal of the Pancreas*, *7*(4), 372–381. https://www.researchgate.net/profile/David-Kooby-2/publication/6953786_Image-Guided_Radiation_Therapy_IGRT_in_Gastrointestinal_Tumors/links/584e07fc08ae4bc899331729/Image-Guided-Radiation-Therapy-IGRT-in-Gastrointestinal-Tumors.pdf

Ragde, H. (2004). Modern prostate brachytherapy. In *Management of Prostate Cancer: Advances and Controversies* (pp. 205–226). CRC Press. https://doi.org/10.3322/canjclin.50.6.380

Roth, A. K., Ris, M. D., Orobio, J., Xue, J., Mahajan, A., Paulino, A. C., Grosshans, D., Okcu, M. F., Chintagumpala, M., & Kahalley, L. S. (2020). Cognitive mediators of adaptive functioning outcomes in survivors of pediatric brain tumors treated with proton radiotherapy. *Pediatric Blood and Cancer*, *67*(2). https://doi.org/10.1002/pbc.28064

Samlowski, W. E., Watson, G. A., Wang, M., Rao, G., Klimo, P., Boucher, K., Shrieve, D. C., & Jensen, R. L. (2007). Multimodality treatment of melanoma brain metastases incorporating stereotactic radiosurgery (SRS). *Wiley Online Library*, *109*(9), 1855–1862. https://doi.org/10.1002/cncr.22605

Sánchez-Parcerisa, D., Kondrla, M., Shaindlin, A., & Carabe, A. (2014). FoCa: A modular treatment planning system for proton radiotherapy with research and educational purposes. *Physics in Medicine and Biology*, *59*(23), 7341–7360. https://doi.org/10.1088/0031-9155/59/23/7341

Schefter, T. E., Kavanagh, B. D., Timmerman, R. D., Cardenes, H. R., Baron, A., & Gaspar, L. E. (2005). A Phase I trial of stereotactic body radiation therapy (SBRT) for liver metastases. *International Journal of Radiation Oncology Biology Physics*, *62*(5), 1371–1378. https://doi.org/10.1016/j.ijrobp.2005.01.002

Schneider, U., Pedroni, E., & Lomax, A. (1996). The calibration of CT Hounsfield units for radiotherapy treatment planning. *Physics in Medicine and Biology*, *41*(1), 111–124. https://doi.org/10.1088/0031-9155/41/1/009

Simpson, D. R., Lawson, J. D., Nath, S. K., Rose, B. S., Mundt, A. J., & Mell, L. K. (2010). A survey of image-guided radiation therapy use in the United States. *Cancer*, *116*(16), 3953–3960. https://doi.org/10.1002/cncr.25129

Skaarup, M., Lundemann, M. J., Darkner, S., Jørgensen, M., Marner, L., Mirkovic, D., Grosshans, D., Peeler, C., Mohan, R., Vogelius, I. R., & Appelt, A. (2021). A framework for voxel-based assessment of biological effect after proton radiotherapy in pediatric brain cancer patients using multi-modal imaging. *Medical Physics*, *48*(7), 4110–4121. https://doi.org/10.1002/mp.14989

Sonke, J. J., Aznar, M., & Rasch, C. (2019). Adaptive Radiotherapy for Anatomical Changes. In *Seminars in Radiation Oncology* (Vol. 29, Issue 3, pp. 245–257). https://doi.org/10.1016/j.semradonc.2019.02.007

Surucu, M., Yeginer, M., Kavak, G. O., Fan, J., Radosevich, J. A., & Aydogan, B. (2012). Verification of dose distribution for volumetric modulated arc therapy total marrow irradiation in a humanlike phantom. *Medical Physics*, *39*(1), 281–288. https://doi.org/10.1118/1.3668055

Vanderwaeren, L., Dok, R., Verstrepen, K., & Nuyts, S. (2021). Clinical progress in proton radiotherapy: Biological unknowns. In *Cancers* (Vol. 13, Issue 4, pp. 1–16). https://doi.org/10.3390/cancers13040604

Vergalasova, I., Liu, H., Alonso-Basanta, M., Dong, L., Li, J., Nie, K., Shi, W., Teo, B. K. K., Yu, Y., Yue, N. J., Zou, W., & Li, T. (2019). Multi-institutional dosimetric evaluation of modern day stereotactic radiosurgery (SRS) treatment options for multiple brain metastases. *Frontiers in Oncology*, *9*(JUN). https://doi.org/10.3389/fonc.2019.00483

Xing, L., Thorndyke, B., Schreibmann, E., Yang, Y., Li, T. F., Kim, G. Y., Luxton, G., & Koong, A. (2006). Overview of image-guided radiation therapy. *Medical Dosimetry*, *31*(2), 91–112. https://doi.org/10.1016/j.meddos.2005.12.004