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Advances in Technology in Radiation Oncology

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Advances in Technology in Radiation Oncology

Mehmet Ufuk Abacioglu

Abstract: The last decade has shown breathtaking developments in radiotherapy. As a local and organ-preserving method, radiation oncology as a discipline is changing its paradigm to more sophisticated, precise treatments rather than large-field irradiations. A radiation beam is more like a scalpel in the era of hypofractionated and ablative doses. It becomes increasingly possible to escalate the fractional and total doses without increasing toxicity; toxicity may even decrease. While early clinical results with these new technologies are very satisfactory, evidence-based long-term results are anticipated. **Eur Assoc Neurooncol Mag 2012; 2 (1): 11–4.**

Key words: radiotherapy, radiation oncology, neurooncology, radiosurgery

Introduction

For many decades, radiation has been one of the main weapons against tumours located in the central nervous system as well as in many other sites. It has potentially curative and ablative effects not only on malignant tumours but also on benign tumours and vascular malformations. Beginning with the radium and kilovoltage X-rays, technological developments have made radiotherapy an essential component of therapy [1]. While the first revolutionary development were Cobalt machines and linear accelerators to treat deep-seated tumours, there has been an evolution of computer and imaging technologies over the last 30 years. Transition from 2-D treatments to 3-D and nowadays 4-D has been possible with CT, MR, and PET imaging. Irregularly shaped targets can be better irradiated using 3-D conformal and intensity-modulated beams. Stereotactic radiosurgery and radiotherapy have been widely adopted in daily practice with the aim of precise and accurate ablative treatments, making it possible to shorten many treatments and to improve patient comfort. Image guidance during treatment has been an important component for these highly precise techniques. Orthogonal X-rays, in-room CT and cone beam CT are examples for right targeting during treatment.

This review aims to cover recent technological developments of radiotherapy targeting central nervous system (CNS) diseases.

Intensity-Modulated Radiotherapy

With the use of CT, 3-dimensional (3-D) visualization of the patient anatomy has been possible and 3-D-conformal radiotherapy has been widely used in almost any treatment site. It has the advantage of improving dose conformity around the target and of sparing adjacent normal tissues compared to conventional radiotherapy fields. Intensity-modulated radiotherapy (IMRT) is a more sophisticated method to deliver highly conformal radiotherapy and its use has been largely common especially in head, neck, prostate, and brain tumours in proximity to critical structures. The basis for IMRT relies on an inverse-planning system, which optimizes delivery of non-uniform beam fluences from multiple directions to allow the intended dose to reach the target with maximal sparing of normal tissues. The treatment system involves use of multileaf collimators that divide each beam into many small beamlets, which are each modulated such that the overall beam intensity patterns achieve the desired target coverage and critical tissue sparing. IMRT treatment for high-grade gliomas has allowed for improved target conformity without increasing the integral dose and volume of normal tissue exposed to low doses of radiation [2].

Helical tomotherapy, developed by Tomotherapy, Inc, as a dedicated rotational IMRT system with a slip-ring rotating gantry, achieves more efficient delivery by continuous gantry rotation and treatment couch translation (Figure 1). It has the advantage of spiral IMRT treatments without the problem of intersecting fields [3].

Linear accelerator vendors have released the capability to vary the angular dose rate by dynamically changing dose rate and/or gantry speed during arc delivery. This new capability, referred to as volumetric-modulated arc therapy (VMAT), has likely spurred a re-emergence of clinical interest in the use of arc therapy. An advantage of VMAT is the potential reduction in delivery time compared with IMRT [4]. A 200-cGy fraction dose can be delivered within 1.5–3 min with VMAT [5]. Varian with RapidArc and Elekta has the commercially available VMAT softwares being used in their linear accelerators

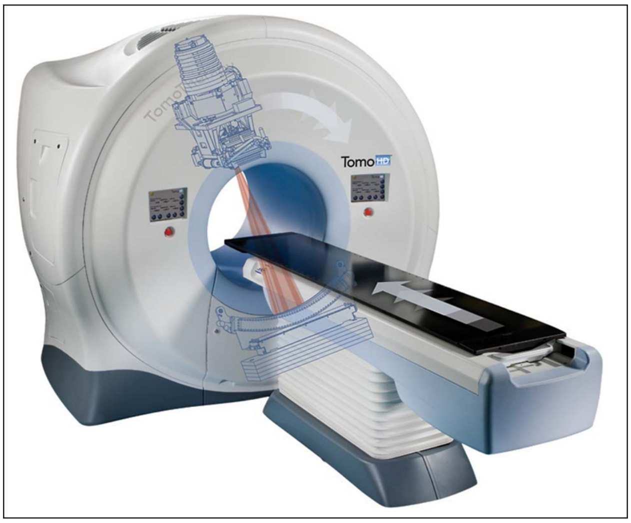

Figure 1. Novel radiotherapy and radiosurgery platforms: TomoHD Tomotherapy. Image used with permission from Accuray Incorporated.

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and treatment planning systems. RapidArc treatment planning and delivery of integrated plans of whole-brain radiotherapy (WBRT) and boosts to multiple brain metastases is a rapid and accurate technique that has a higher conformity index than conventional summation of WBRT and radiosurgery boost [6]. With this technique it is feasible to treat both the macroscopic metastases to a higher dose and the microscopic disease with a lower prophylactic dose at the same time (Figure 2). Another novel technique is hippocampus sparing during whole-brain radiotherapy, aiming at the reduction of neurocognitive complications of whole-brain irradiation [7]. It is possible to reduce the median dose for the hippocampus to 5–8 Gy, while other parts of the brain receive 30 Gy.

With the advent of precise radiation techniques, the role of prophylactic irradiation both in primary brain tumours (like glioblastoma) or metastases has been questioned. Even in the concurrent temozolomide era, local in-field recurrences are still the majority. Recent studies show that a 1-cm clinical target volume expansion to the contrast-enhancing areas might result in the same local recurrence rate as a 2–3-cm margin [8]. For patients with a limited number of metastases, radiosurgery alone results in the same overall survival as with the addition of whole-brain irradiation [9].

The proton beam has a very advantageous physical character. It has a very rapid dose fall-off at the range. However, its dependence on a large particle accelerator, which is very expensive to build, has prevented the technique from being widely used. There is ongoing research by several companies to construct proton machinery with smaller accelerators, and at an affordable price to make this highly conformal treatment accessible to larger populations.

Stereotactic Radiosurgery and Hypofractionated Radiotherapy

Since Leksell's conception of stereotactic radiosurgery, technology has proliferated and radiosurgery has become a standard procedure in the treatment of many benign and malignant CNS pathologies [10]. Radiosurgery relies on 3-D or stereotactic image localization, thereby enabling co-identification of a virtual target in the treatment-planning computer with the actual target position for treatment delivery [11]. The first Gamma Knife containing 179 Co-60 sources became operational in Stockholm in 1968. It was redesigned using 201 Co-60 sources arranged in a hemispherical configuration to create a more spherical dose distribution. Treatment is performed by positioning the patient's tumour in the centre of the focused radiation. Models B and C were developed to facilitate reloading of the Co-60 sources and patient positioning. The Perfexion model has 192 Co-60 sources arranged in a cylindrical configuration in 5 rings (Figure 3) [12]. The new repositioning head frame, "Extend", facilitates fractionated treatments and extends the treatment fields to the cervical and upper neck regions as well.

Cyberknife is a compact X-band linear accelerator mounted on a 6-axis robotic arm (Figure 4) [13]. The multi-axis robotic arm allows the positioning of the linear accelerator in any direction and at various surface-to-axis distances. With a complex planning process to choose the optimal beam configura-

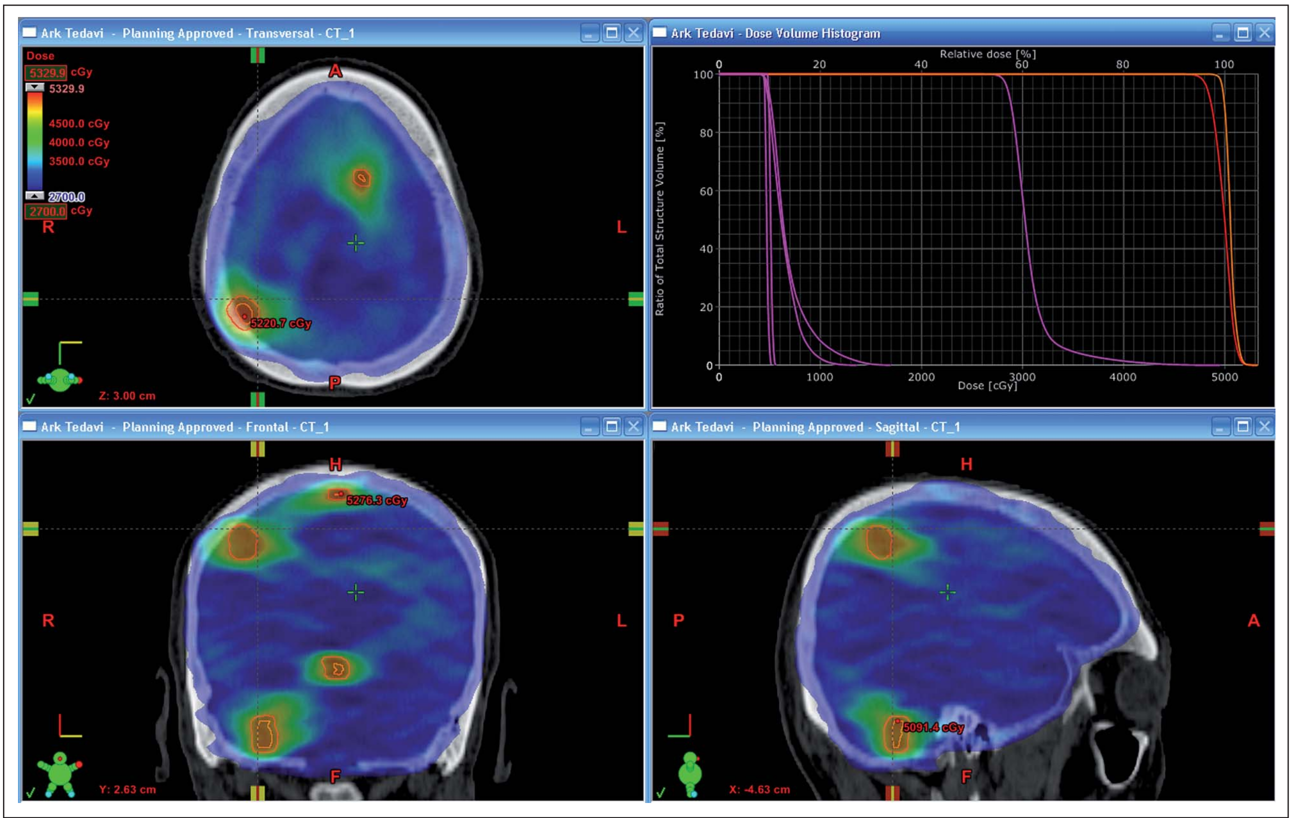

Figure 2. Whole-brain radiotherapy with integrated boost for multiple metastases. The whole brain receives 30 Gy in 10 fractions, while the boost dose to the macroscopic tumours is 50 Gy.

Figure 3. Novel radiotherapy and radiosurgery platforms: Gamma Knife Perfexion. Courtesy of Elekta.

tions and beam weights, automated procedures help physicians and physicists. Diagnostic X-rays mounted to the ceiling enable real-time orthogonal image guidance without the need for a stereotactic frame. Bony structures or implanted radio-opaque markers allow the localization of the target. The dynamic tracking software, Synchrony, allows to follow the target in moving parts of the body.

In recent years, linac-based radiosurgery manufacturers have also developed high-technology linear accelerators to specifically deliver radiosurgery more accurately and efficiently [14–16]. All of the linacs currently marketed for radiosurgery share common features: higher dose rates, integrated image guidance, integrated high-resolution multi-leaf collimation, and improved mechanical accuracy [11]. The first example was Clinac 600SR by Varian, a dedicated radiosurgery accelerator with a single 6-MV energy with a 10×10 cm maximum field size [17]. Later on, Varian's partnership with BrainLab improved linac-based radiosurgery technology. Besides circular collimators, computer-controlled m3® micro-multileaf collimators (mMLC) with a 3-mm projection at the beam isocentre allowed for beam-shaping and intensity-modulated radiosurgery. Image guidance on the Novalis systems is performed by the fully integrated ExacTrac X-Ray 6D, which consists of 2 infrared cameras for patient prepositioning and tracking, 2 floor-mounted X-ray tubes, and 2 ceiling-mounted amorphous silicon flat panel detectors for X-ray image guidance. These components allow for computer-assisted infrared and X-ray-based correction and verification of the patient's position before and during treatment. Varian has extended the radiosurgery partnership to Trilogy and Novalis TX high-energy linear accelerators which are also equipped with cone beam CT, allowing for the acquisition of soft-tissue imaging for image guidance. Similarly, both Elekta and Siemens have marketed radiosurgery linacs featuring higher dose rates, higher accuracy, high-resolution mMLCs, and CBCT for soft-tissue image guidance (Figure 5).

Traditional radiosurgery uses an invasive headring for stereotactic localization and minimization of motion during image acquisition and treatment. Taking into account the disadvantages of frame-based invasive systems, several frameless systems have been developed. They rely on optical and/or image guidance. Thermoplastic masks are used for immobilization. Extracranial radiosurgery (eg, of the spine) has also become an effective and more frequently used treatment to increase the effectiveness of radiation treatment for tumours in close proximity to very critical structures such as the spinal cord.

Figure 4. Novel radiotherapy and radiosurgery platforms: Cyberknife. Image used with permission from Accuray Incorporated.

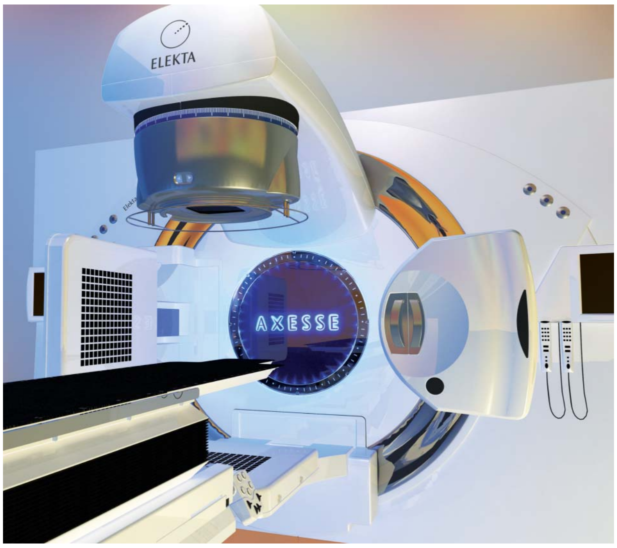

Figure 5. Novel radiotherapy and radiosurgery platforms: Elekta Axesse. Courtesy of Elekta.

In recent years, there has been increasing interest in flattening filter-free (FFF) linacs [18]. It is possible to expect a reduction in the out-of-field dose due to reduced head scatter and residual electron contamination, which results in a benefit for normal tissues because of decreased scatter doses [19]. Removal of the flattening filter may also provide delivery of the dose up to 4 times faster. Besides its treatment efficiency, radiobiological implications of increased dose rates are investigated [20]. The first commercially available system is TrueBeam from Varian. After integration of the TrueBeam linac with the Novalis ExacTrac imaging and positioning system, a 6-dimensional couch and high-definition multi-leaf collimators were added to further improve the precision of radiosurgery and SBRT (Figure 6).

As a result of these flexible platforms for any type of radiotherapy, it has been possible to use different fractionation

Figure 6. Novel radiotherapy and radiosurgery platforms: TrueBeam STX with Novalis. Image courtesy of Varian Medical Systems, Inc. All rights reserved.

regimens from multiple fractions to single-fraction treatments. Large tumours in the brain that cannot be irradiated in a single fraction now have the option to be irradiated with hypofractionated treatments. Using the accurate imaging, it has been possible for some tumours to shorten overall treatment time by means of hypofractionation.

■ Image-Guided Radiotherapy

Detailed anatomical imaging in CNS has been one of the most important milestones for treatment of CNS tumours. Revolutionary change has been made by the implementation of 3-dimensional imaging with soft tissue visualization of the body by CT and MR. Modern treatment planning softwares have the capability of registering and fusing MR and CT image sets, which significantly enhances the accuracy of target delineation [21]. Aminoacid and hypoxia tracers for PET/CT, besides new MR techniques like diffusion, perfusion, and spectroscopy, have added metabolic information to the anatomical delineation [22]. They are useful for target delineation, dose-painting, and evaluation of disease progression. Although rather investigational at the moment, delineation of nerve fibre tracts and shape of dose according to this information allow for the radiation oncologist to decrease the possible complications of radiotherapy, just like its use in neuro-oncology [23].

A potential source of inaccuracies in the treatment of patients relates to the difficulty in daily repositioning of the patient within the immobilization device in exactly the same way [21]. Image-guided radiotherapy (IGRT) is visualization of the target and the normal structures just before and during treatment and correction of the potential set-up errors. Different vendors have different on-board imaging (OBI) solutions for image guidance. Orthogonally paired X-ray images can be compared to the digitally reconstructed radiographs (DRR) which are created from the simulation CT to check the set-up accuracy and to correct positioning errors. Cone beam CTs, integrated to the modern linacs, make it possible to image the soft tissues in-room and correct positioning according to the verification of registered images with the planning CT scan.

For extracranial treatments, respiratory motion is an important component of intrafractional motion. 4-D CT simulation makes it possible to have images at different phases of respiration and to contour the target and critical structures separately. Gating, active breath control, and tracking are contemporary methods, both to increase the accuracy of treatment and to decrease the volume and dose applied to critical structures.

■ Conclusions

Radiotherapy is an important part of the standard of care for many CNS tumours. Recent technological advances have enhanced our targeting accuracy, thereby reducing unnecessary, so far normal tissue doses. New technologies have also provided the possibility to shorten the fractional and overall treatment times, which is an improvement regarding patient comfort and quality of life. Integration of systemic and targeted therapies with novel radiotherapy technologies is investigated for their synergistic interactions.

■ Conflict of Interest

MUA has no conflict of interest to declare.

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