Advances in Technology in Radiation Oncology

Abacioglu U

European Association of NeuroOncology Magazine 2012; 2 (1) 11-14

Homepage:

www.kup.at/journals/eano/index.html

Online Database Featuring Author, Key Word and Full-Text Search

Member of the

Krause & Pachernegg GmbH · VERLAG für MEDIZIN und WIRTSCHAFT · 3003 Gablitz, Austria
**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 multi-leaf 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.
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.](image-url)
tions and beam weights, automated procedures help physi-
cians and physicists. Diagnostic X-rays mounted to the ceil-
ing 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 specifi-
cally 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 accel-
erator 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 cir-
cular 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 per-
formed 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 guid-
ance. 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-en-
ergy 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 stereo-
tactic localization and minimization of motion during image
acquisition and treatment. Taking into account the disadvan-
tages of frame-based invasive systems, several frameless sys-
tems 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 prox-
imity to very critical structures such as the spinal cord.

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 re-
sidual electron contamination, which results in a benefit for
normal tissues because of decreased scatter doses [19]. Re-
moval of the flattening filter may also provide delivery of the
dose up to 4 times faster. Besides its treatment efficiency, ra-
diobiological implications of increased dose rates are investi-
gated [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-di-
mensional 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 radio-
therapy, it has been possible to use different fractionation
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. Revolution 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-ranking, 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 intracranial fractionation. 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.

References: