The idea of artificial people can be traced to the ancient Greek myth of Cadmus and later to the first recorded designs of a humanoid robot by Leonardo da Vinci (Fig. 1). The word “robot” was introduced by Czechoslovakian writer Karel Capek in his play R.U.R. (Rossum’s Universal Robots), which premiered in 1920. The name was coined by Capek’s brother Josef, who derived it from the noun robota, which means “forced labor or drudgery” in Czechoslovakian. Many consider the first truly modern robot to be the teleoperated boat (similar to a modern remotely operated vehicle) devised by Nikola Tesla and subsequently demonstrated at an 1898 exhibition at Madison Square Garden. The word “robotics” was first used in print by Isaac Asimov, in his science fiction short story “Runaround,” which appeared in 1941. Simultaneously, in the 1930s and 1940s, further advancements in technology allowed the development of the robots Elektro and Elsie (Bristol Tortoise), although it was not until 1960 that the first truly modern robot, the Unimate, was produced and actually commissioned into industrial use.

The invention of the cyclotron (Fig. 2) by Ernest Lawrence in 1929 and its subsequent improvements, along with Robert Wilson’s 1946 proposal to use charged particles for clinical use, made the device the primary choice at that time for “therapeutic radiation”—a therapeutic modality introduced at the end of the 19th century by German physicist Wilhelm Röntgen and frequently utilized by Marie Curie in her work with x-rays, polonium, and radium. Lars Leksell’s invention of the arc-quadrant stereotactic system in 1949 further cemented the ability of clinicians and scientists to accurately target selected areas in the brain. Leksell and Borje Larsson subsequently introduced the concept of radiosurgery. By the end of the 1950s and 1960s, the use of cyclotrons and later synchrotrons in a clinical setting was well established. In 1967, Leksell and Larsson developed and successfully introduced the Gamma Knife, which they subsequently and effectively utilized to treat a variety of intracranial tumors. These modalities remained primary in radiosurgery until the development of the LINAC system by Betti et al. and Co-lombo et al. in the 1980s and the subsequent invention of the CyberKnife system by John Adler and colleagues in 1997.

Image Guidance and Robotics
The key to the activation and utilization of any robot in radiosurgery is accuracy in imaging. In this regard, radiosurgery has evolved in parallel with the progress in imaging technologies and computers. Current conformal plan-
ning techniques coupled with an ability to deliver a maximal dose to the tumor while sparing surrounding structures has become more efficient and accurate. Magnetic resonance imaging, including functional magnetic resonance imaging, perfusion-diffusion imaging, spectroscopy, and diffusion tensor imaging, as well as single-photon emission CT and positron emission tomography has contributed to the definition of the planning target volume. The introduction of IMRT \(^\text{17}\) in 1992 has made it possible to tailor the distribution of the dose according to the often nonhomogeneous lesion shape or complex geometry and the presence of surrounding critical structures.

Patient positioning has also become extremely critical given that the methods and devices currently in use are increasingly considered inadequate to deliver sophisticated treatment plans. This insufficiency is primarily due to natural internal organ motion, such as that during respiration, which can have a profound effect on the precision of radiation delivery.

Image-guided radiation therapy \(^\text{13,38}\) is the process by which images of the body are captured immediately before treatment delivery. These images can be produced via numerous methods including fluoroscopy, radiography, or cone beam tomography. The images are subsequently fused or matched with treatment planning images by using computer software to detect and correct movements of the organs or to compensate for displacement of the target due to natural movements or other physiological conditions.

Three-dimensional conformal radiotherapy \(^\text{16,19,24,31}\) is a process that begins with the creation of individualized, 3D digital data sets of tumors and normal adjacent anatomy. These data sets are then used to generate 3D computer images and to develop complex plans to deliver highly conformed radiation while sparing healthy adjacent tissue. These advancements allow further modification of target plans to increase accuracy and specificity, which in turn allows the utilization of a higher radiation dose while decreasing the amount of radiation exposed to the normal surrounding tissues.

**Radiation Sources and Robotic Devices**

Currently, three major sources of radiation are utilized in current radiosurgery devices: gamma rays, x-rays, and sub-
atomic particles such as electrons, protons, and neutrons. Only gamma rays and x-rays are currently used in true robotic devices, and consequently they will be considered in this article.

**Gamma Rays and the Gamma Knife**

The gamma rays utilized in radiosurgery are photon beams produced by radioactive decay, which interact with the corona of electrons of the atoms that compose the irradiated tissue and thereby ionize them. Gamma rays are produced by fixed sources of radioactive $^{60}\text{Co}$ and are used exclusively in the Gamma Knife device (Fig. 3), which was invented by Leksell and Larsson in 1967. Since then, according to its parent company Elekta, the device has been used in the treatment of > 400,000 patients. Because of its extensive use and the enormous amount of supportive data generated, the Gamma Knife is still considered the gold standard for intracranial radiosurgery.

The Gamma Knife consists primarily of a hemispheric array of 201 $^{60}\text{Co}$ sources that are collimated to the center. Magnetic resonance imaging and CT scanning of the target and positioning of the patient are achieved with reference to the Leksell stereotactic headframe (Fig. 4), which is firmly applied to the patient’s skull, and by using the propriety computer software GammaPlan, which allows for accurate target selection. The fixed spatial relationship between the frame and the target structure is identified via localizers applied to the frame during pretreatment image acquisition. All of these factors translate into precise targeting of the lesion once the frame is positioned for treatment. The target is placed at the center of the collimated sources to ensure that optimal treatment is delivered. When the shape of the target is not spherical, treatment is usually accomplished through a process that utilizes a cluster of spherical lesions that cover the irregularly shaped volume to be treated.

In later versions of this system, a robot (Cartesian) has been incorporated with the aim of positioning the frame during treatment, so that each shot or spherical radiation dose can be automatically and precisely directed in sequence to the target. In the latest version of this device, named Perfexion, the hemispheric collimator array (Fig. 5) has been completely enveloped into the main housing assembly, which prevents patient discomfort, and is controlled automatically by on-board computers programmed according to the treatment and target plans. This automation reduces the need for manual input and errors. The whole dose-delivery process, including patient positioning, is now completely automated, allowing seamless workflow and reducing treatment time.

The Gamma Knife has some limitations in its use: only cranial and cervical lesions can be treated, and the dose distribution to the target lacks homogeneity. Furthermore, treatment can only be delivered during a single session and therefore dose fractionation, when multiple doses are given over multiple treatment sessions, cannot be utilized.

**Radiography and LINAC Applications**

In the early 1980s LINAC radiosurgery was introduced by Betti et al. and Colombo et al. This procedure utilizes x-rays, which are photon beams produced by electron acceleration. This concept of multiple noncoplanar arc therapy has been complemented in the last decade with the development of multileaf and micromultileaf collimators. Whether built into the LINAC head or added as an accessory, these multiaxial robots allow highly conformal and uniform doses to be delivered to the target. Additionally, they can modulate the intensity of the dose according to treatment requirements.

The dosimetric performance of some of these devices, particularly those claimed to incorporate better design characteristic such as double focusing, interdigitation of blade travel, thinner leaves, dynamic movements, minimal transmission, and leakage between the leaves, is very high and inferior only to that of proton beam therapy and Tomo...
Charged particle beam dosimetry is in fact superior to any other photon therapy method and can be very effectively shaped by electromagnetic steering. Unfortunately, access to this treatment modality is currently out of reach for the majority of radiation oncologists as there are presently only a few centers worldwide that offer it, although this situation is rapidly changing.

Applications of LINAC Radiosurgery

Integrated features on current x-ray–based devices such as the On-Board Imager, a feature of Varian Trilogy (Fig. 6), consists of a low-energy x-ray tube and an amorphous flat panel detector facing the tube, on either side of the patient. These components are mounted on articulated motorized arms and generate diagnostic-quality projection images of the patient. Advantages of the new device consist of the potential for high-quality image acquisition, optimal acquisition geometry with respect to the target, speed, and a lower radiation dose to the patient. Images are compared with the treatment planning images, and appropriate patient positioning corrections are made.

Two-dimensional projection imaging is adequate when the target lies close to osseous structures and its position is unaffected by respiratory or other physiological movements or by gravity. This scenario typically applies to the brain, for which the skull serves as a stereotactic frame and, to a lesser extent on occasion, the contents of and the area immediately adjacent to the spinal canal.

To visualize soft tissue, metal or fiducial markers can be implanted and then imaged prior to treatment with radiography. Still, 2D imaging doesn’t provide sufficient information especially during movement of the target. To offset this problem, a solution has been offered by Varian’s On-Board Imager and PortalVision (both components of Trilogy), by Elekta’s VolumeView (a component of Synergy), and by other companies that have equipped their latest accelerators with CT-quality imaging by using cone beam technology. With this ability, several hundred images can be acquired in a single 360° rotation.

The result is a 3D image of soft tissue, but when the tumor to be treated lies in the lungs or in organs adjacent to the diaphragm, the 4th dimension (time) must be visualized. Asking the patient to hold his or her breath at a specific cycle (that is, deep inspiration) during treatment, instructing him or her to breathe only when treatment is stopped, or using physical restraints for the chest can be very demanding, especially for patients with limited respiratory capacity.

A different solution has been created based on the description of chest or abdomen movement during breathing, obtained with optical tracking of fiducial markers applied to the skin, and monitored by infrared cameras. The waveform of the patient’s breathing pattern is synchronized with the CT image acquisition so that gating of the radiation beam can be automatically performed by the cameras during treatment when they detect the position of the markers that correspond to the position of the tumor in the field chosen for treatment. Radiation gating is well utilized by most complex LINAC devices including Varian’s Trilogy (which incorporates the RPM respiratory gating system) and Elekta’s Synergy (which incorporates its MotionView technology).
Another IGRT approach is Helical TomoTherapy, which combines a rotating-intensity modulated fan beam on a helical ring gantry with integrated CT scanning. This method of imaging the body during treatment was first described by NOMOS Corporation\textsuperscript{10,26,30} in 1997 but was successfully applied only later by Mackie\textsuperscript{26} and colleagues\textsuperscript{27} and Fitchard and associates\textsuperscript{14} after the introduction of spiral CT. The result was highly integrated adaptive radiotherapy, a procedure that provides a combination of real-time image guidance and IMRT by using a binary multi-leaf collimator.

As the ring gantry of this device rotates in simultaneous motion with the treatment couch, helical fan-beam IMRT is continuously delivered from all angles around the patient while CT scanners acquire hundreds of very narrow images with each gantry rotation. The width of the fan beam and the maximum length the treatment couch are extensive enough to allow very large volumes to be treated in a single set-up. A similar concept has been implemented in the GammaStar Gyro Knife, which combines a Gamma Knife and LINAC system. This device is currently in the research and development stage, but it would be interesting to study its effects.

Significant clinical follow-up data documenting the benefits related to the introduction of these novel technologies are not yet available, but the combination of IMRT, IGRT, and 3D conformal radiotherapy promises improved tumor control and superior sparing of normal tissue. These benefits are achievable with a lower complication rate, a shorter treatment time, and frequently a lower instrument cost.

**CyberKnife Robotic Radiosurgery System**

Approximately 1 decade ago, CyberKnife (Accuray; Fig. 7) was introduced into clinical practice.\textsuperscript{1,2} It was the first device for precision radiotherapy that utilized an industrial robot to train a photon beam generated by a small on-board LINAC directly to the target. Some of its advantageous features not offered by other devices include unobstructed access to the entire body, high mechanical precision, and an innovative, ingenious image-guided control loop with target-tracking capabilities, which allows the user to perform real-time tracking and thus obviates the use of invasive frames to stabilize the patient.

Although it uses the same basic principle as the Gamma Knife system in terms of delivering targeted therapy, the CyberKnife has numerous differences. It covers the target with a nonisocentric array of beams of high conformity rather than the multiple-shot treatment delivered by the Gamma Knife. Significantly, the CyberKnife is an “open” system and therefore allows unobstructed treatment of the whole body rather than just the head and neck.

Now in its fourth generation, the CyberKnife system incorporates a miniature lightweight 6-MV LINAC, with

---

**Fig. 8.** Screenshot from CyberKnife treatment computer demonstrating real-time mapping of the patient position by using “synthetic images” (left column) and x-ray “camera” images (middle column). The final digital reconstructed “overlay” images (right column) are produced by overlapping the computer and x-ray images, which allows correction of patient positioning and subsequent accurate deployment of the robot arm and treatment beam. The variation in position and subsequent required corrections can be seen in the lower portion of the image. The treatment plan can also be visualized in the image, which demonstrates the number of nodes used and the dose desired and delivered simultaneously.
circular secondary collimators of various diameters, mounted on an industrial robot (KUKA Roboter GmbH) with 6 degrees of freedom for movement. Treatment planning with this device is similar to other inverse planning systems: Note that identification of the target and critical structures surrounding it based on pretreatment morphological and functional data sets, prescription of the target dose, and description of any constraints are all performed using the propriety Multiplan and InView software.

A CT scan as well as other appropriate studies is mandatory to generate pre- and intratreatment digitally reconstructed neuroimages and is essential for patient positioning and subsequent tracking.

Planning of dose delivery is performed in a unique fashion: the system chooses a number of nodes that lie on a sphere, some 80 cm around the target volume. Guided by the dose and the constraints applied, the system chooses beam directions and weights for each node to reach optimal conformity with the planned dose distribution. Therefore, this nonisocentric technique is nearly at a par with the submillimeter accuracy of the Gamma Knife system in designing highly conformal plans; significantly, it also accommodates wrap-around doses and techniques to treat critical structures like the spinal cord in the treatment of spinal metastases.

A unique feature of the CyberKnife system is represented by the image-guided loop (Fig. 8). Two flat-panel amorphous silicon x-ray cameras are used for real-time patient positioning and treatment tracking. The system generates a sequence of digitally reconstructed radiographs from the pretreatment CT, which are matched with the orthogonal x-ray images acquired during treatment. The new target position is then compared with the target position at the planning phase, and the beam directions are corrected accordingly. This process is the reason why noninvasive stabilization of the patient during therapy can be performed.

Various additions to the system have been introduced since its conception. In principle, the frameless approach gives more choices in beam-angle selection compared with those offered by radiosurgery with a frame. Of course, the robotic arm must avoid collision with the patient, table, and imaging system and direct beam incidence into the imaging system. Another area of concern is the long treatment time compared with that of other delivery systems like the Gamma Knife (Table 1). Although the Gamma Knife currently provides accuracy that cannot be matched by the CyberKnife, its limited ability to treat noncervical lesions, the need for frame fixation, and increased treatment time with the CyberKnife mean that the Gamma Knife holds promise not only as a radiotherapeutic tool, but also as a neurosurgical tool. Although its underlying principles that are affected by respiration such as those in the lung, liver, and pancreas, without the application of breathing or gating techniques. Utilizing fiber optics, the Synchrony system enables patients to breathe normally throughout their treatment while maintaining accuracy and minimizing damage to the surrounding healthy tissue. This real-time detection is cross-checked by the system via digitally reconstructed radiographs to accommodate the robot’s final position prior to treatment delivery.

Another addition, the Xsight tracking system, uses internal anatomy to directly track targets with accuracy and precision without the need for external frames or implanted fiducial markers. Currently, this technology is available only for the treatment of the lung and spine.

The CyberKnife, with its various developments, is a device that truly represents the evolution of a concept originating in the Gamma Knife system, but one that has been revolutionarily improved upon by the concurrent advancements in imaging, computers, and robotic research.

**Conclusions**

Radiosurgery is a special radiotherapy technique that holds promise not only as a radiotherapeutic tool, but also as a neurosurgical tool. Although its underlying principles are similar to those of conventional radiation therapy, the accuracy requirements in dosimetry, targeting, and patient positioning for radiosurgery are at the submillimeter level. These stringent requirements are now achievable because of the evolution of devices and concurrent advances in the fields of electronics, imaging, and computers. These improvements, in turn, have served to advance the robotic industry to the extent that these devices are now accessible for radiosurgical applications.

A robotic device such as the CyberKnife mounted on a robotic arm with 6 degrees of freedom or a combined device like the TomoTherapy Hi-Art system are more universal in terms of their ability to move to any part of the human body compared with a device with limited degrees of freedom such as the Gamma Knife (Table 1). Although the Gamma Knife currently provides accuracy that cannot be matched by the CyberKnife, its limited ability to treat noncervical lesions, the need for frame fixation, and no means of dose fractionation have led to increased enthusiasm for the CyberKnife. On the other hand, the complicated robotic movements, treatment plans, and increased treatment time with the CyberKnife mean that the Gamma Knife...
Robotics and its applications in stereotactic radiosurgery

Knife, with its long-standing proven treatment history, will still be utilized for cranio-cervical treatments and will for the immediate future remain the gold standard in intracranial radiosurgery.

Nevertheless, it will be interesting to observe the coming changes in the field of radiosurgery, as robots with ≥ 7 degrees of freedom, combination devices such as TomoTherapy, and improved imaging and computing capabilities will further evolve and improve the radiosurgery process and eventually fulfill the concept of “intelligent radiosurgery.”

References


Address correspondence to: Lawrence S. Chin, M.D., Department of Neurosurgery, Boston Medical Center, 720 Harrison Avenue, Doctors Office Building, Suite 7600, Boston, Massachusetts 02118. Email: lawrence.chin@bmc.org.