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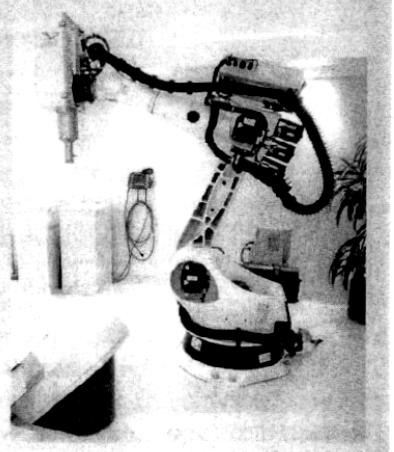
THE CYBERKNIFE STEREOTACTIC RADIOSURGERY SYSTEM: DESCRIPTION, INSTALLATION, AND AN INITIAL EVALUATION OF USE AND FUNCTIONALITY

The CyberKnife Stereotactic Radiosurgery System is manufactured by Accuray, Inc. (570 Del Rey Avenue, Sunnyvale, CA 94085; telephone 1-888/522-3740 or 1-408/522-3740; http://www.accuray.com). It is currently available for purchase (capital cost of US $3.2 million plus US $0.5 to 0.75 million for site setup), or in a revenue-sharing plan (US $0.5 to 0.75 million setup cost).



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The CyberKnife Stereotactic Radiosurgery System (SRS) incorporates recent technological advances in robotics and computerized image recognition to achieve an innovative quantum leap in radiosurgery. The CyberKnife mounts a lightweight linear accelerator (LINAC) on an industrial robotic arm that accurately and efficiently delivers radiotherapy while being guided in real time by advanced computer image tracking technology in a frameless environment (1). The CyberKnife, which is now being adopted worldwide, was developed by Dr. John Adler, Jr., along with his colleagues at Stanford University and Accuray, Inc. It was approved in 2001 by the United States Food and Drug Administration for use in radiotherapy of lesions anywhere in the body. The University of Southern California-Norris Cancer Hospital unit is one of the first United States installations of the newest, second-generation CyberKnife, and our initial experience is described in this review.

The current CyberKnife SRS configuration includes a 6-megavolt (MV) LINAC (weight, 120 kg) attached to a computer-driven robot arm with six degrees of freedom, two ceiling-mounted diagnostic x-ray cameras with corresponding orthogonal, floor-mounted amorphous silicon detectors for real-time digital imaging, and a treatment couch with electronic controls for five degrees of freedom (x, y, and z axes, head tilt, and left-right rotational axes) with one manually adjusted clockwise-counterclockwise rotational degree of freedom that is based on the position of the patient. An operational advantage is that there are no permanent radiation sources that require periodic replacement or additional safety and licensing requirements.

To ensure successful implementation, the radiosurgery team (consisting of neurosurgeons, radiation oncologists, neuroradiologists, radiation physicists, radiation therapy technicians, and nurses) should have clinical expertise and experience in the fundamental principles and practice of stereotactic radiosurgery. A 2-day rudimentary training course is offered by Accuray, Inc., to orient all team members with the operational specifics of the CyberKnife and facilitate initial startup. Continuing education updates are available and may be given on site by Accuray technical and associated staff. Direct technical support and

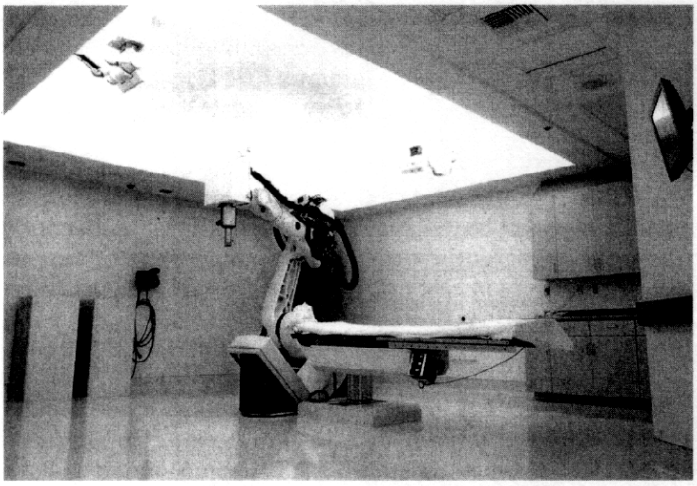

FIGURE 1. *Photograph illustrating the CyberKnife SRS installation at the University of Southern California-Norris Cancer Hospital: robot arm and LINAC, treatment couch, ceiling-mounted x-ray cameras, and floor-mounted amorphous silicon detectors.*

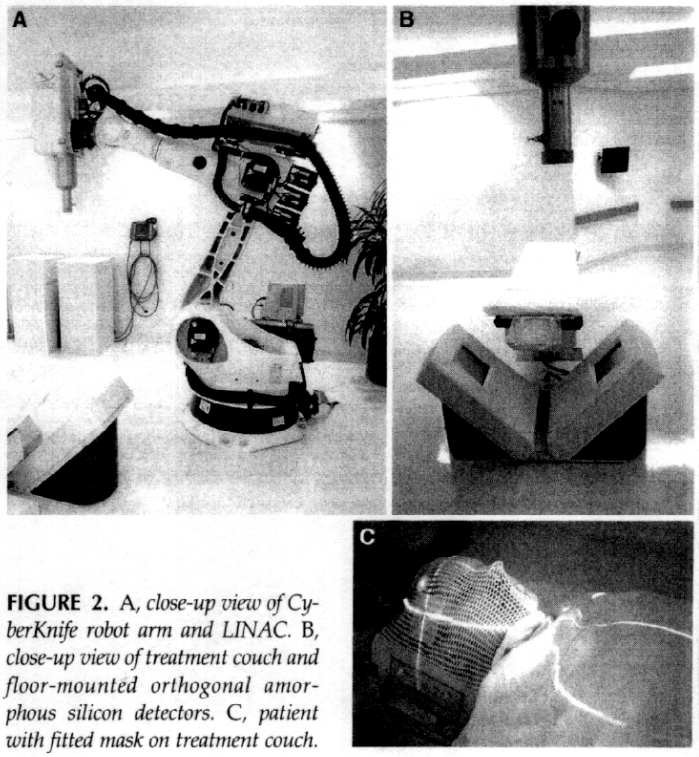

FIGURE 2. A, *close-up view of CyberKnife robot arm and LINAC.* B, *close-up view of treatment couch and floor-mounted orthogonal amorphous silicon detectors.* C, *patient with fitted mask on treatment couch.*

customer service are available from Accuray, Inc. The newly inaugurated CyberKnife Society promises to be a forum for information exchange by users worldwide.

In consultation with the purchasing institution, specialized staff from Accuray are closely involved in planning for new CyberKnife installations. There are multiple flexible installation plans, and the minimal physical requirements for a CyberKnife installation are as follows: 1) the treatment area should have a recommended 48-inch equivalent concrete shielding in all six walls and should meet local shielding requirements needed to satisfy site usage and government regulations; 2) the flooring should support at least 6000 lb of weight (consisting of CyberKnife LINAC and robot, 3500 lb; treatment couch, 1000 lb; and ancillary equipment and personnel); 3) an 11-ft ceiling is required over a 12- × 16-ft area centered on the treatment couch; 4) the location should have a sufficient electrical power supply for the CyberKnife unit (150 amps, 208 V) and associated computing and ancillary peripherals.

We installed our unit in an existing LINAC facility after floor excavation to accommodate the robotic arm's height and installation of shielding as required (*Fig. 1*). Our subcontractors finished the facility retrofit and construction in 6 weeks. CyberKnife SRS installation and testing by Accuray was completed in 4 weeks. Radiosurgical sessions are directed via a computer workstation and monitored by closed-circuit cameras in an adjacent shielded control room. The system power generator, robotics and planning computing platforms, and data storage hardware are in a separate support room. We also have a secondary computer workstation for treatment planning when the primary workstation is occupied during treatment. All computers and imaging facilities are connected in a high-speed network to facilitate rapid image and treatment plan transfers.

The CyberKnife couples flexibility and accuracy with patient comfort and convenience via the following features. This system's dynamic tracking software (DTS) can directly track a patient's cranium in six dimensions (three translational and three rotational axes) to target intracranial lesions in true frameless stereotactic radiosurgery; a conventional stereotactic frame fixed to a patient's head is not needed. Furthermore, for extracranial lesions, small radiopaque fiducial markers (2- × 5-mm steel screws for spinal applications, 0.5- × 5-mm gold seeds for extracranial applications) placed near targets are tracked as reference points during treatments. The robot arm-mounted LINAC has expanded maneuverability as a result of an available six degrees of freedom and the range to reach along a treatment couch that is similarly mobile (*Fig. 2A*). The current LINAC generates up to 4 Gy/min radiation dosing via 6-MV photon beams that are regulated by 12 available collimators (ranging in size from 5 to 60 mm).

Optimal stereotactic radiosurgical plans treat lesions with beams positioned to intersect and maximize target radiation and minimize damage to adjacent normal tissue because of rapid dose falloff. Theoretically, CyberKnife has the potential to create a nearly infinite number of radiation beams by firing from all points in space around the patient (with only small areas excluded as a result of imaging considerations). In practice, the present CyberKnife SRS can fire from 101 specific nodes in space, each with 12 approach angles, thus offering up to 1212 possible beams for extensive treatment flexibility. Both isocentric and nonisocentric treatment plans are possible as a result of this feature, and the CyberKnife can also achieve a high target conformability and dose homogeneity for irregu-

larly shaped lesions. Targets defined on pretreatment patient imaging (computed tomography, magnetic resonance imaging, and computed tomographic angiography) are used to generate customized treatment plans with user-directed forward or inverse planning via the CyberKnife planning software on sophisticated computer workstations.

Targeting accuracy coupled with real-time correction via image guidance during radiosurgery is a unique feature of the CyberKnife SRS. It is frequently described as akin to the military technology of "smart" cruise missiles whereby the surrounding terrain is continually compared to stored maps to keep the missile on target. Pretreatment imaging is used to generate three-dimensional landmarks (via anatomic features or implanted fiducial markers) on digitally reconstructed radiographs (DRR) for computer comparison with x-ray images obtained serially during the course of a treatment. The two amorphous silicon detectors rapidly generate fully digital, distortion-free x-ray images in orthogonal orientations (*Fig. 2B*). Deviations of these x-ray images (obtained in real time during treatments), as compared with the DRR, are displayed graphically as the root-mean-square (RMS) error. The computer-driven robot will automatically correct for up to 10 mm of translation and/or 5 degrees of rotational motion found during comparisons, but human operators may interrupt a treatment if the RMS error graph is trending upward before the maximum CyberKnife correction tolerance is met. In addition, measurements obtained during simulated treatments indicate that the CyberKnife's absolute accuracy for dose delivery to desired targets deviates no more than 1 to 1.5 mm from ideal throughout a treatment. Because of its engineered intrinsic accuracy and the dynamic capability to correct for possible target motion, CyberKnife treatment readily allows for accurate and reproducible dose delivery via fractionation schemes to treat larger lesions and minimizes damage to critical structures. Patient comfort and convenience are served by eliminating invasive frame placement. In addition, because imaging and planning can occur at any time before the radiosurgery procedure, the coordination of radiological resources, physician schedules, and patient needs is simplified. This also improves the efficient use of the radiosurgery team resources.

CLINICAL EXPERIENCE

In a 5-month period, we treated 81 patients in 212 fractions after our CyberKnife SRS unit was activated on October 21, 2002. The treated lesions included intracranial tumors (metastases, meningiomas, pituitary tumors, acoustic neuromas, glomus jugulare tumors), head/neck cancers, spinal metastases, pulmonary lesions, and metastases to extremities. We started treating selected patients with arteriovenous malformations in May 2003. The existing radiosurgery team (consisting of neurosurgeons, radiation oncologists, neuroradiologists, radiation physicists, radiation therapy technicians, and nurses) is often expanded to involve thoracic surgeons, hepatobiliary surgeons, otolaryngological surgeons, ophthalmologists, interventional radiologists, and other specialists in the planning and execution of extracranial treatments. With the addition of the CyberKnife unit, we still maintain an active gamma knife radiosurgery program by triaging patients and lesions most suited for each modality. In general, larger (>3 cm), peripheral, or poorly accessible cranial base intracranial lesions are selected for CyberKnife treatment, along with a fast-growing referral of selected patients with extracranial lesions.

A typical treatment paradigm for intracranial or head/neck lesions is the following: the selected patient comes for pretreatment computed tomography with intravenous contrast 1 day before starting treatment. He or she is first custom-fitted with an immobilizer face mask on the treatment couch and then wears the newly made mask for the computed tomographic scan (*Fig. 2C*). The target is delineated on the obtained images and used for treatment planning with the physician-prescribed constraints (dosing and fractionation schedule). It usually takes our experienced radiation physicists approximately 1 hour to generate an optimal treatment plan, with a time range of 15 minutes to several hours depending on the shape and number of targets and the complexity of constraints. This compares favorably with the planning time required for other radiosurgical modalities.

When the patient returns for treatments, he or she lies on the treatment couch with the immobilizer mask and is manually maneuvered to register actual patient anatomy detected via x-ray images with the DRR generated from the pretreatment computed tomographic imaging. Once patient positioning is determined by human operators to be within the correction threshold (ideally <1 mm translation and/or 1 degree of rotation) of the CyberKnife DTS, the treatment is started. During each treatment session, the DTS automatically monitors for patient movement and adjusts the robotic arm accordingly, and the continuously measured RMS error is graphically displayed throughout the treatment for operators. The rate of radiation dose delivery is monitored by two built-in ion chambers and is also displayed for quality control. At our facility, quality assurance is performed before the first treatment each day by measuring and calibrating LINAC dose delivery. From the control area for each treatment, we observe robot arm motion for proximity to the patient on four different closed-circuit cameras deployed in the treatment room. The CyberKnife is able to interrupt a treatment (E-stop) on the basis of a wide range of error conditions. Most notable are those leading to unsafe conditions, such as a potential collision with the patient or excessive patient movement that may result in inaccurate targeting. Human operators may also manually interrupt a treatment and then set it to resume automatically after desired adjustments are made. If a treatment is aborted, make-up plans are automatically generated by the robust CyberKnife DTS system, so interrupted treatments are easily continued at any time. Most patients undergo convenient outpatient treatment sessions that are completed within 1 hour, and they complete a treatment plan of two to five fractions in the same number of days.

For patients with extracranial lesions, the fundamental principle is to introduce three or more adjacent radiopaque fidu-

cial markers that maintain a fixed relationship to the lesion to achieve accurate targeting. Selected patients with spinal lesions receive percutaneously implanted spinal fiducial markers (in fixed bony elements) under fluoroscopic guidance as outpatients, at least 2 days before pretreatment imaging. The reasons for the time delay are to reduce pain when the patient lies down for imaging and treatment and to decrease swelling-related tissue distortion that causes targeting inaccuracy. For patients with selected pulmonary lesions, we use gold seeds contained in endobronchial catheters as fiducial markers placed via bronchoscope before imaging; we then perform planning and treatment the same day to minimize patient discomfort. Endobronchial catheters are removed immediately after treatment, and patients stay overnight in the hospital for observation. Other methods are also being developed for fiducial placement in CyberKnife treatment of visceral targets. No procedure-related complications have ensued from our minimally invasive fiducial placements.

For the treatment of extracranial lesions, patients are usually positioned on a bean bag on the treatment couch to facilitate access and avoid collision with any mobile part of the CyberKnife (collimator, LINAC, robot arm) during treatments. One feature of the planning software is a simulation of the robot arm's complete excursions during the entire treatment to detect and eliminate positions that intrude into patient space; still, it is imperative for human operators to closely monitor each treatment session for such potential collisions. In addition, once the DTS is properly recognizing implanted fiducial markers, it can also ascertain whether there is excessive fiducial migration, indicating possible loss of targeting accuracy, and stop treatment for operator evaluation and adjustment.

In conclusion, the CyberKnife SRS is a major evolutionary advance in radiosurgery instrumentation that combines sophisticated robotics and computerized image guidance to offer real-time target adjustment in a frameless stereotactic environment, thereby achieving efficacy and accuracy while maximizing patient comfort and convenience. It expands the range of possible lesions that can be treated via radiosurgery beyond the cranium and provides an exciting template for future developments in radiosurgery technology.

APPRAISAL AND RECOMMENDATIONS

As with any new technology or procedure, there is no substitute for experience gained in the course of CyberKnife use. We recommend that intracranial lesions be the first attempted treatments with a new CyberKnife. Most radiosurgery teams are familiar with treating intracranial lesions, and the cranium's easily recognizable anatomic features on x-ray images will facilitate patient registration with the DRRs. It is straightforward to recognize and correct developing errors that are the result of patient motion during the course of treatment by changes in the cranium registration with DRRs, usually also illustrated in RMS error graphs. The staff will also develop expertise in mask fitting, treatment couch manipulation, and patient positioning to set up treatments.

Fiducial recognition and registration with the CyberKnife DTS pose another level of complexity and sophistication best tried after more experience with the CyberKnife SRS. Although the CyberKnife DTS is an excellent image recognition software package, it sometimes fails to recognize fiducial markers that are easily observed on x-ray images by the human eye. In those cases, manual fine-tuning of both the imaging and display parameters can sometimes improve fiducial marker recognition, which suggests that more improvements in the DTS algorithm are desired. Frequently, human operators need to change or delete fiducial markers to assist in completion of a treatment plan as a result of intra- or inter-session changes in patient positioning or fiducial migration in tissues. Cognitive skills and judgment learned by operators in previous CyberKnife treatments will facilitate proper setup and smooth treatments in complicated cases.

We have noted several possible improvements to achieve higher potential efficiency and patient throughput. The custom-fit face mask or bean bag scheme for immobilizing patients is not always reproducible between treatment planning and multiple treatment sessions, leading to excessive setup time spent on manual patient positioning. A remote control for the treatment couch would also facilitate position changes and decrease time for setup or correction after E-stops. Another source of inefficiency is that occasionally, when a treatment is paused or aborted, the robot arm must be manually reset to its starting ("perch") position, and then it must inefficiently traverse all previous positions before resuming treatment. In addition, the CyberKnife robot arm does not take the most parsimonious mechanical path in its excursions, stopping at nodes even if no energy is being delivered.

Some of these problems are being corrected in the new "Express" upgrade package of enhancements just installed at our facility. Rather than being performed in sequence, both image registration and robot arm movement are speedily executed during treatments by means of parallel processing. The CyberKnife no longer needs to return to perch before resuming paused treatments, and stop times at nonactive nodes are now minimized. Upgrades to the LINAC hardware will increase the rate of dose delivery and further decrease treatment time.

We found Accuray's customer service to be superbly responsive and available. They helped diagnose and replace a crashed hard drive, then reinitialize and test the entire CyberKnife SRS system within 1 day after a power failure. Several repairs of the treatment couch and electronic controls were coordinated with gaps in treatment schedule or on weekends to avoid disruption of patient treatments. Technical staff members are easily reached to troubleshoot and diagnose problems by telephone; they will immediately review plans by Internet and suggest potential solutions in concert with our team even during treatments.

ALTERNATIVE UNITS

There are no other radiosurgery instruments that have the capabilities of the CyberKnife SRS to perform frameless ste-

reotactic radiosurgery with real-time targeting for lesions throughout the human body.

REFERENCE

1. Adler JR Jr, Murphy MJ, Chang SD, Hancock SL: Image-guided robotic radiosurgery. **Neurosurgery** 44:1299–1307, 1999.

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COMMENTS

The article is a straightforward and enthusiastic description of the University of Southern California-Norris Cancer Hospital group's early experience with the CyberKnife. Previous articles have described first-generation CyberKnife systems. This group has concisely summarized current CyberKnife technology, and they specifically address some of the changes intrinsic to the second-generation CyberKnife model. The outline of installation considerations and logistical concerns is particularly useful for anyone considering investment in CyberKnife technology.

Insights regarding the system's safety and efficiency are helpful. Kuo et al. quantify the times spent by their physicists in dose planning and by the patients in treatment times; however, from a neurosurgeon's perspective, description of the neurosurgeon's component of treatment planning would be of interest as well. The issue of fiducial implantation has become an area of interest within radiosurgery for extracranial treatments. A more detailed description of the complexities of fiducial placement that the authors have encountered would be welcomed to steepen the learning curve as more extracranial sites are tackled.

Radiosurgery has become an increasingly important topic in the neurosurgical literature. Understanding the various platforms is critical for making important investment decisions on which future treatment options will be based. The CyberKnife is an extremely promising new technology. As with any novel technology, the CyberKnife has minor flaws and limitations, which are being identified and resolved more rapidly as a result of the sharing of insights by groups such as this one.

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Kuo et al. critically review their initial experience with the installation, setup, and clinical use of new radiosurgery equipment, the final evolution of the modified linear accelerator and gamma knife, the CyberKnife. This comprehensive article provides valuable information for neurosurgeons as well as radiation oncologists.

The CyberKnife makes it easy to immobilize the patient, and its features permit interrupted procedures to be easily reinitiated. Lesions larger than 3 cm and irregularly shaped lesions can be treated. The treatment of tumors located near critical areas, such as spinal cord or paraspinal cord tumors, is possible. The CyberKnife offers new opportunities in efficient tumor care by means of an unconventional radiation therapy fractionation scheme.

Kuo et al. point out the urgency of good team cooperation to optimize the use of this sophisticated equipment: it can be used satisfactorily for radiotherapy treatment of visceral moving targets, such as lung, liver, pancreas, and prostate. As confirmed by Kuo et al., the CyberKnife expands the range of possible lesions that can be treated via radiosurgery and provides an exciting template for further development. Moreover, the possibility of fractionated two to five "single-shot" sessions of radiation may change the whole concept of radiosurgery and may herald a new philosophy of therapy for cranial base and spinal tumors.

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Intensity-modulated radiation therapy has made it possible to use linear accelerators to treat tumors with higher doses safely and effectively in many sites that could not previously be treated by radiosurgery. Quality intensity-modulated radiation therapy requires a high degree of certainty regarding reliable and precise treatment planning, patient setup, and treatment verification. The concept of an image-guided miniature linear accelerator mounted on a robotic arm is both elegant and appealing. Enthusiastically described in this article, CyberKnife projects greater reliability in treatment planning and delivery with a greater degree of flexibility than is possible with more traditional linear accelerators and patient immobilization schemes.

Despite the large number of patients treated, this study lacks sufficient data to support the claims made regarding the accuracy of the treatment planning system and comparisons to the current, standard intensity-modulated radiation therapy paradigm. Although the concept is simply stated, it is, in reality, an extremely complex machine. One significant limitation may be the size of the linear accelerator that can be mounted on a robotic arm. Are we really willing to embrace a new idea without knowing how well it works? Modern radiation therapy demands a high level of certainty and reliability to ensure that treatment is given as intended. Proof of treatment planning and verification with excellent patient outcomes in terms of local tumor control and neurological preservation are essential to safe and effective use of this new technology.

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