

A STUDY OF THE ACCURACY OF CYBERKNIFE SPINAL RADIOSURGERY USING SKELETAL STRUCTURE TRACKING

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OBJECTIVE: New technology has enabled the increasing use of radiosurgery to ablate spinal lesions. The first generation of the CyberKnife (Accuray, Inc., Sunnyvale, CA) image-guided radiosurgery system required implanted radiopaque markers (fiducials) to localize spinal targets. A recently developed and now commercially available spine tracking technology called Xsight (Accuray, Inc.) tracks skeletal structures and eliminates the need for implanted fiducials. The Xsight system localizes spinal targets by direct reference to the adjacent vertebral elements. This study sought to measure the accuracy of Xsight spine tracking and provide a qualitative assessment of overall system performance.

METHODS: Total system error, which is defined as the distance between the centroids of the planned and delivered dose distributions and represents all possible treatment planning and delivery errors, was measured using a realistic, anthropomorphic head-and-neck phantom. The Xsight tracking system error component of total system error was also computed by retrospectively analyzing image data obtained from eleven patients with a total of 44 implanted fiducials who underwent CyberKnife spinal radiosurgery.

RESULTS: The total system error of the Xsight targeting technology was measured to be 0.61 mm. The tracking system error component was found to be 0.49 mm.

CONCLUSION: The Xsight spine tracking system is practically important because it is accurate and eliminates the use of implanted fiducials. Experience has shown this technology to be robust under a wide range of clinical circumstances.

KEY WORDS: CyberKnife, Image-guided robotic radiosurgery, Spinal tumors, Spine

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Radiosurgery combines the principles of stereotactic localization with multiple cross-fired beams from a collimated radiation source and enables a very large, highly conformal dose of radiation to be safely targeted at a well-defined pathological lesion in one or, at most, a limited number of sessions with the goal of achieving local ablation (23). The CyberKnife (Accuray, Inc., Sunnyvale, CA) radiosurgery system provides a mechanism whereby treatment beams can be precisely aligned with radiosurgical targets without the use of stereotactic frame fixation. This technical approach results in several fundamental differences from conventional frame-based radiosurgical systems. First, the CyberKnife references the position of the target to internal radiographic anatomy or implanted fiducials rather

than a stereotactic frame. Second, it periodically acquires x-ray images to establish the position of the lesion during radiosurgery, and then dynamically brings subsequent beams of radiation into alignment with the observed position of the target. According to this concept, offsets in patient position are not accepted as setup errors, as is largely true with conventional radiation therapy, and attempts are not made to restrict patient movement through rigid skeletal immobilization, as is the case with standard stereotactic radiosurgery. Instead changes in patient position during radiosurgery are compensated for by adaptive beam pointing. As a consequence, a patient can be positioned comfortably throughout radiosurgery without the necessity of precisely reproducing the pose that was obtained in the

treatment planning imaging study. Third, the CyberKnife aims each beam independently, without a fixed isocenter.

Stereotactic radiosurgery is an accepted treatment for many types of intracranial lesions. The CyberKnife was originally developed to perform radiosurgery throughout the brain and head and neck regions (1). The outcomes of CyberKnife treatment for intracranial lesions have closely mirrored the results of conventional, frame-based radiosurgery (3, 4, 25, 31). Conventional devices for intracranial radiosurgery use skeletal fixation to immobilize a target at a known location in space and do not have the capability of treating lesions below the foramen magnum. Unlike frame-based systems, the CyberKnife can treat lesions outside the cranium. There is a large and growing interest in using this technology to treat tumors throughout the body, including the spine, lung, prostate, liver, and pancreas (27). In particular, the application of radiosurgery to spinal lesions represents a logical extension of radiosurgical principles. The pathology of the vast majority of spinal tumors is identical or similar to those found in the brain; most lesions have a fixed specific position relative to bony anatomy (i.e., vertebrae), and the combination of high conformality and high accuracy enables a very large dose of radiation to be delivered to the lesion while minimizing the dose to the spinal cord. Early results with spinal tumors treated by CyberKnife radiosurgery have been promising. Akin to intracranial radiosurgery, recent reports have documented low rates of complications and high rates of tumor control for benign spinal tumors, as well as excellent pain relief and tumor control in patients with spinal metastases (2–4, 7, 8, 12–22, 33, 34, 36).

Until recently, the standard method used by the CyberKnife to treat lesions within the lower cervical, thoracic, and lumbar spine involved fiducial-based targeting. For this technique, radiopaque fiducials, which serve as radiographic landmarks, are implanted percutaneously into the posterior elements of the vertebrae adjacent to the lesion being treated. Because insertion takes place before the acquisition of the treatment planning computed tomographic (CT) image and because the markers have a fixed relationship with the bone in which they are implanted, the fiducials provide an internal frame of reference. Using at least three non-collinear fiducials, the tracking system compares the positions of the fiducials in the treatment planning CT scan and the orthogonal x-ray images, thereby determining the position and orientation of the radiosurgical target. Fiducial-based targeting is fast, accurate, and robust (38). However, marker implantation adds an invasive procedure to an otherwise non-invasive treatment. In response to this limitation, a recently developed software product called the Xsight Spine Tracking System (Accuray, Inc.) localizes spinal targets strictly by directly tracking adjacent skeletal structures, thereby eliminating the need for implanted fiducials.

Because spinal lesions are often located adjacent to or even within the radiation-sensitive spinal cord, a thorough knowledge of the accuracy of the Xsight spine tracking system is of special importance and forms the underlying rationale for the current investigation. To achieve this objective, targeting error was measured using a realistic, anthropomorphic head-and-

neck phantom. Total system error, which is the geometric error in the delivery of the planned dose distribution, is defined for the purpose of this study as the distance between the centroids of the planned and delivered dose distributions. Importantly, this value measures all possible errors intrinsic to the relatively complex process of image-guided robotic radiosurgery, including the tracking system, the CT scanner, the treatment planning software, the robot, and the linear accelerator. In a more clinically relevant situation, the tracking system contribution to total system error was determined in isolation by retrospectively analyzing image data from 11 patients with implanted fiducial markers who underwent CyberKnife radiosurgery for a range of spinal pathology.

METHODS

CyberKnife Radiosurgery System

The CyberKnife radiosurgery system has been described previously in detail (1, 6). In summary, an image-guided targeting system is combined with a mechanism for precisely delivering high-energy radiation. A miniature lightweight X-band linear accelerator provides a source of 6 MV therapeutic radiation. The linear accelerator is coupled to a multijointed robotic manipulator that is capable of accurately aiming the radiation beam with six degrees of freedom. The CyberKnife targeting system uses two diagnostic x-ray generators that are mounted to the ceiling of the CyberKnife treatment room to illuminate two approximately orthogonal amorphous silicon x-ray detectors, which generate high-resolution digital images. The x-ray generators and detectors are rigidly fixed and their projection camera geometry is calibrated and known with very high accuracy in the treatment room coordinate system. After an initial course alignment performed by the operator, computer algorithms automatically compare the projection images of the target region taken from the perspective of the two x-ray cameras with the patient's treatment planning CT scan. Using image registration methods, the spatial coordinates of the radiosurgical target are computed and relayed to the robotic manipulator, which compensates automatically for small movements of the target by realigning the radiation beam generated by the linear accelerator.

At the start of a CyberKnife treatment, the x-ray image-guided tracking system is used to align the patient with the assistance of an adjustable five-axis treatment table. The sixth axis, which is the "yaw" rotation, is adjusted by manually repositioning the patient with respect to the table. During treatment, x-ray image acquisition and target localization are repeated periodically (typically about once per min). The robotic manipulator compensates for small translations and rotations. Rotations of more than a few degrees automatically pause treatment and prompt the operator to reposition the patient before proceeding.

Xsight Spine Tracking System

The target pose (position and orientation) is determined using image registration. The pair of two-dimensional (2D)

x-ray projection images is registered to the pretreatment three-dimensional (3D) CT scan, in which the target and therapy beams have been defined. Xsight spine tracking uses intensity-based (as opposed to fiducial-based) 2D-3D image registration. This approach involves generating synthetic x-ray images, or digitally reconstructed radiographs (DRRs), by casting rays through the CT scan using the known x-ray camera geometry. The 2D-3D image registration method determines a set of geometric transformation parameters that optimizes a similarity measure that quantitatively compares the DRR and x-ray images. Registration-based target localization is called tracking because it is repeated periodically during treatment.

Most published intensity-based 2D-3D image registration methods iteratively vary the pose of the CT scan, generating DRRs for each pose (24, 29, 30, 32, 35). This search process is continued until a similarity measure that globally compares the DRR and x-ray images is optimized. The Xsight algorithm differs from these published methods in several fundamental ways. First, a 2D-2D registration between an x-ray image and the corresponding DRR image is performed independently for each projection. The direction of inference is reversed by estimating the 3D transformation from the measured 2D in-plane transformations (the 2D transformation parameters are components of the 3D transformation parameters). Second, the 2D in-plane transformations are computed using local displacements of skeletal structures rather than a global similarity measure. Finally, to accurately estimate local displacements of skeletal structures, the skeletal features in the DRR and x-ray images are enhanced before registration. Many of the technical details have been presented elsewhere (10, 11). A brief summary is presented here.

To a good approximation, the x-ray imaging process can be modeled as a linear attenuation of x-rays as they pass through an object. This ignores the effects of scatter and beam hardening. The DRR is generated by ray casting through the CT scan. The integral of the linear attenuation coefficients along each ray is approximated as the sum of the linear attenuation coefficients derived from the CT values of each voxel encountered along the ray. Trilinear interpolation of CT values is used to improve the integral approximation. The incident x-ray intensity is proportional to the exponential transformation of the negative integral of the linear attenuation coefficients. Ray casting is performed for every pixel in the DRR. The resulting DRR is enhanced using postprocessing filters, including Gamma correction and top-hat filtering (10). The x-ray image is similarly enhanced. The effect of image enhancement is illustrated in *Figure 1*. Image enhancement emphasizes the skeletal structures in the images and improves the estimate of local displacements of these structures.

A 2D-2D registration between an x-ray image and the corresponding DRR image is performed independently for each x-ray projection image. The registration is performed in a region of interest (ROI) that includes the anatomy that will be treated. The ROI is centered about a manually specified CT scan coordinate system origin, which is generally on the anterior surface of the spinal canal in the mid-sagittal plane and at the vertical

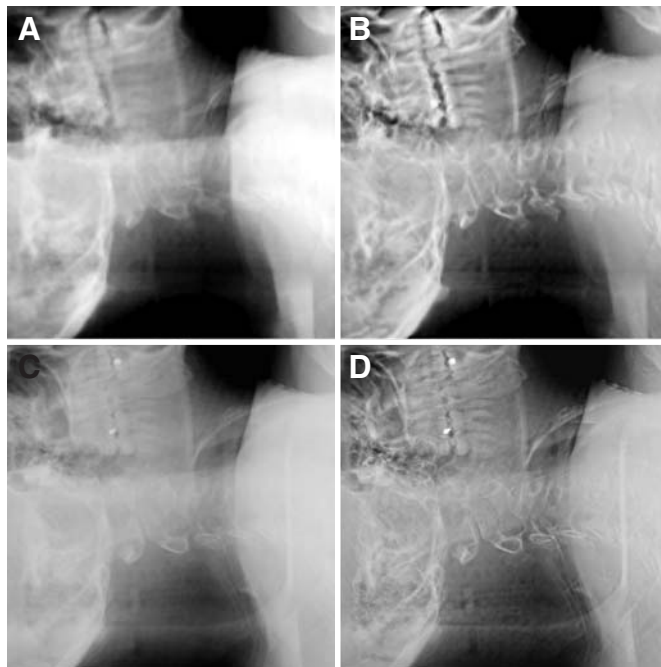


FIGURE 1. The effect of image enhancement for a cervical spine patient. A, original digitally reconstructed radiograph image, which is a synthetic x-ray image generated by casting rays through the CT scan using the known x-ray camera geometry. B, DRR image after image enhancement. C, original x-ray projection image. D, x-ray image after image enhancement. Image enhancement emphasizes the skeletal structures in the images and improves the estimate of local displacements of skeletal structures during the 2D-2D registration between an x-ray image and the corresponding DRR image.

mid-point of the vertebral body. The size of the ROI is manually defined and generally includes the vertebra of interest plus the two adjacent vertebrae. In the occasional circumstances in which adjacent bony anatomy may be unduly mobile and, therefore, unreliable skeletal landmarks (e.g., the mandible in the case of some cervical lesions), it can be advantageous to not “center” the ROI on the vertebrae of interest.

The local displacement vector that aligns a point in the DRR image with the corresponding point in the x-ray image is estimated at each node point in a grid or mesh laid over the ROI. Each node point is the intersection of two grid lines in the mesh. The displacement vector is determined by translational block matching. A small region (block) surrounding the node point in the DRR image is compared with regions in the x-ray image. The intensity pattern in this small region represents local skeletal structure. The displacement is the vector difference between the center of the block in the DRR image and the most similar block in the corresponding x-ray image. The quantitative comparison between blocks is computed using a similarity measure called pattern intensity, which is effective for the registration of skeletal structures in x-ray projection images (30, 35). Block matching, which is essentially the estimation of 2D local displacements of skeletal structure, is performed in a multi-resolution (also known as hierarchical and coarse-to-fine)

approach to improve efficiency (decrease computation time) and robustness (avoid local optima). An approximate estimate of displacement begins at the lowest (coarsest) resolution by using the entire ROI as a block and a large search window. Using these approximate results as initial estimates, the local displacement of node points is estimated in successively higher resolution (finer) grids composed of successively smaller blocks and smaller search windows. Block matching starts with a single block (the entire ROI), which is successively subdivided into 3×3 , 5×5 , and 9×9 grids. Grids on x-ray and DRR images for a lumbar case are shown in *Figure 2*.

The nodal displacement vectors form a 2D displacement field. The position (translation) and orientation (rotation) of the skeletal anatomy, and thus the target, is computed from the two 2D displacement fields (11). The translation and rotation represent a six degree-of-freedom rigid transformation. In summary, the 3D displacement of the CT image coordinate system origin is determined by back-projection of its two 2D displacements. The orientation is determined from the two in-plane rotation angles (which are determined by computing a rigid in-plane transformation from the nodal displacements for each projection) and information in the displacement fields.

Anthropomorphic Phantom Study

The total system error of the CyberKnife system using Xsight spine tracking was measured using an anthropomorphic head-and-neck phantom (Model RS-108T; Radiological Support Devices, Long Beach, CA) containing a film holder (*Fig. 3*). The phantom consists of a cranium and seven cervical vertebrae. The x-ray attenuation of the structures in the phantom and the radiographic appearance of the phantom in CT and x-ray images are comparable to that of a living person. The film holder, or ball-cube, measures 31.75 mm on edge and is constructed of acrylonitrile-butadiene-styrene plastic with a 19-mm diameter acrylic sphere (which has a higher CT number than the surrounding plastic) located in its center. The film holder is made of four identically shaped plastic rectangles; when the film holder is assembled, it holds two pieces of orthogonally positioned radiochromic dosimetry film in a known spatial relationship to the acrylic sphere. To index the position of the film precisely, the edges of the film are aligned with the outer anterior, left, and superior edges of the film holder. The sphere center is within 0.13 mm of the cube center as measured with optical techniques. The film holder is oriented with the radiochromic films placed in the axial and sagittal planes. The film holder is placed in the phantom and together they are imaged in a CT scanner. The sphere is contoured as a target in the CT images of the phantom and a treatment plan is generated using a 15-mm collimator with a specified dose prescribed to an isodose contour corresponding to the surface of the spherical target. Two pieces of radiochromic dosimetry film (GAFChromic MD-22; ISP Technologies, Wayne, NJ) are placed in the film holder and the phantom is irradiated just as in a normal treatment, thereby exposing the film to the planned treatment. The exposed film is read in an optical scanner and the resulting dose distribution analyzed. The

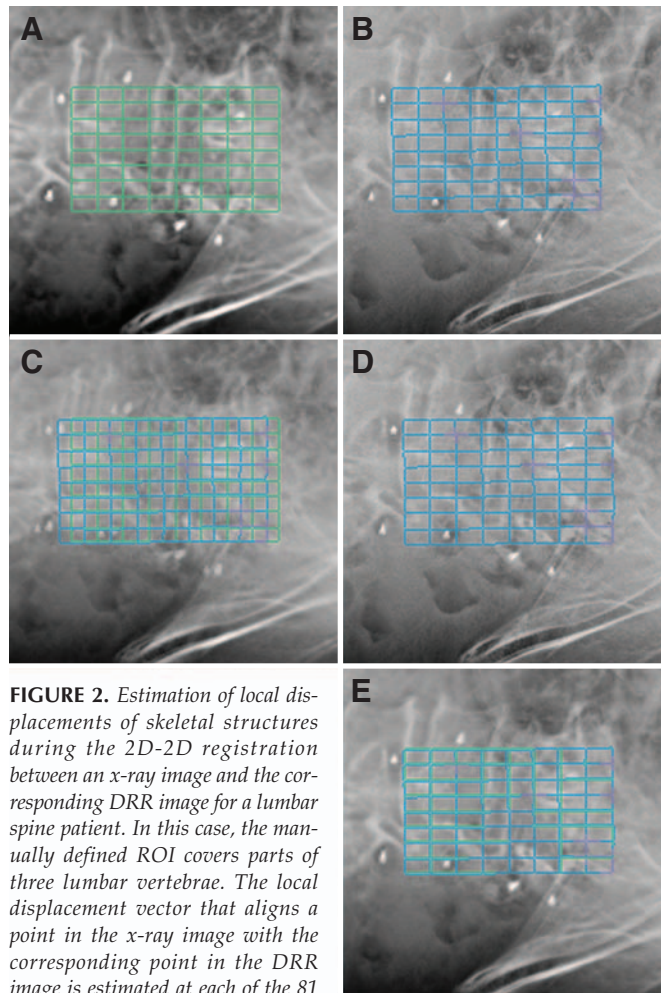


FIGURE 2. Estimation of local displacements of skeletal structures during the 2D-2D registration between an x-ray image and the corresponding DRR image for a lumbar spine patient. In this case, the manually defined ROI covers parts of three lumbar vertebrae. The local displacement vector that aligns a point in the x-ray image with the corresponding point in the DRR image is estimated at each of the 81 node points in a 9×9 regular grid that covers the region of interest. Each node point is the intersection of two grid lines in the mesh. A, DRR image with overlaid grid. B, x-ray image with overlaid grid before initial patient alignment. Each node point corresponds to a node point in the regular grid shown on the DRR image in A and was determined by translational block matching. C, a combination of the DRR and x-ray images with overlaid grids before initial patient alignment. The images are combined by adding the corresponding pixel values. It is visually obvious that the images are in poor alignment. The skeletal features show up in pairs in the combined image. The two grids are misaligned by a horizontal (superior-inferior) translation that is approximately one-half of the grid spacing. D, x-ray image after patient alignment. The treatment table was moved according to the patient misalignment computed by the Xsight tracking system from the 2D displacement fields. E, a combination of the DRR and x-ray images after patient alignment. The combined image is free of the types of artifacts that are seen when images are in poor alignment and the grids are in almost perfect alignment. This figure, as well as Figures 4 and 5, show magnified images from one of the two projection views. The Xsight user interface shows the DRR, x-ray, and combination images for both projection views in a 2×3 layout. The images can be displayed at various magnifications. The grid, the user-defined CT image coordinate system origin, and linked cross-hairs can each be optionally overlaid on the images.

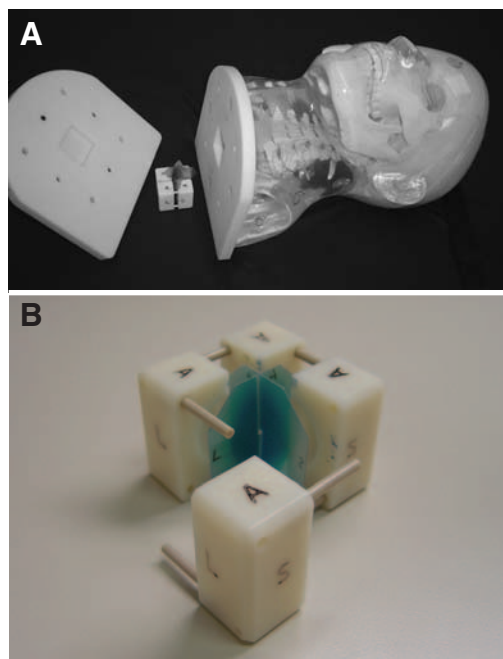


FIGURE 3. Photographs showing the anthropomorphic head-and-neck phantom, film holder, and film used to measure the total system error of the CyberKnife system with Xsight spine tracking. A, anthropomorphic head-and-neck phantom, which consists of a cranium and seven cervical vertebrae. B, partially assembled film holder with two pieces of orthogonally positioned radiochromic dosimetry film.

radiochromic film analysis is similar to that described by Yu et al. (38). The total system error is calculated as the distance between the centroid of the sphere and the centroid of the isodose contour in the exposed film dose distribution corresponding to the surface of the sphere (i.e., the distance between the centroids of the planned and delivered dose distributions).

The film holder and phantom were imaged using a CT scanner (LightSpeed; GE Healthcare, Chalfont St. Giles, United Kingdom). The CT scan acquisition parameters were: voltage, 120 kV; matrix size, 512 x 512 pixels; number of slices, 250; slice thickness, 1.25 mm; no interslice gap; and field of view 250 x 250 mm. Each isocentric treatment incorporated 30–100 beams that delivered a maximum dose of 30 to 40 Gy. The beam weights were optimized in the treatment planning software to make the dose distribution as spherical as possible (because of asymmetry in the distribution of the treatment beam directions, an equally weighted isocentric treatment plan would be relatively less spherical). Delivery of the planned treatment was performed using Xsight spine tracking. The exposed self-developing radiochromic dosimetry film was left to develop for more than one day to ensure complete developing. After developing, the films were scanned optically using a transparency scanner. The film analysis results are relatively insensitive to film response. The analysis computes the centroid of a particular isodose contour. Because the dose distribution is spherical, the centroids of neighboring

isodose contours differ only slightly (tenths of millimeters). Thus, absolute calibration of the film is unnecessary and was not performed.

Clinical Image Data Analysis

Registration is the determination of a one-to-one mapping or transformation between the coordinates in one space and those in another, such that points in the two spaces that correspond to the same anatomic point are mapped to each other. From an operational point of view, the inputs to an image registration algorithm are the two images to be registered; the output is a geometrical transformation. To the extent that corresponding anatomic points are mapped to each other, the registration is successful. If there is an error in the transformation, the anatomic objects will be mapped to an incorrect location. A common way of measuring registration error is to look at the misalignment of points after registration (26, 37). This error measure is generally referred to as target registration error in the medical image registration literature, in which the word “target” denotes that the point represents an anatomic location of surgical or radiosurgical interest (9, 26, 37).

The fundamental process in the tracking system is image registration; thus, the tracking system error component of total system error is equivalent to the target registration error. We computed the Xsight spine tracking system error by retrospectively analyzing clinical image data obtained (with institutional review board approval) from the final 11 patients who underwent CyberKnife treatment for spinal lesions using implanted fiducial markers (i.e., before the Xsight system was installed). Each patient had four implanted fiducials; an example is shown in *Figure 4*. When the patients were treated, the fiducials were used as a geometric frame of reference for targeting the spinal lesions. In the retrospective analysis, each fiducial was used not as a fiducial to compute a registration as would be the case in fiducial-based tracking, but rather as a target to evaluate the intensity-based (fiducial-less) registration performed by the Xsight software. The fiducials were removed from the CT scans (and thus the DRR images) using image processing techniques (“air brushing”) before performing the registration to more realistically simulate the fiducial-less situation and avoid bias in the evaluation of Xsight tracking system error (37). The target registration error (Xsight tracking system error) was computed for each target as the Euclidean distance between the 3D position of the marker in the treatment room coordinate space computed by backprojecting its 2D positions in the x-ray images and its 3D position determined using the six degree-of-freedom rigid transformation produced by the Xsight spine tracking system.

For each patient, the following information was obtained and used to perform the analysis: 1) a pretreatment CT image (slice thickness, 1.25 mm; field of view sufficiently large to image the entire cross section of the body). 2) Approximately 20 to 50 pairs of orthogonal projection x-ray images obtained at intervals of approximately 60 seconds for the duration of treatment. The x-ray images have 512 x 512 pixels with 0.4 mm

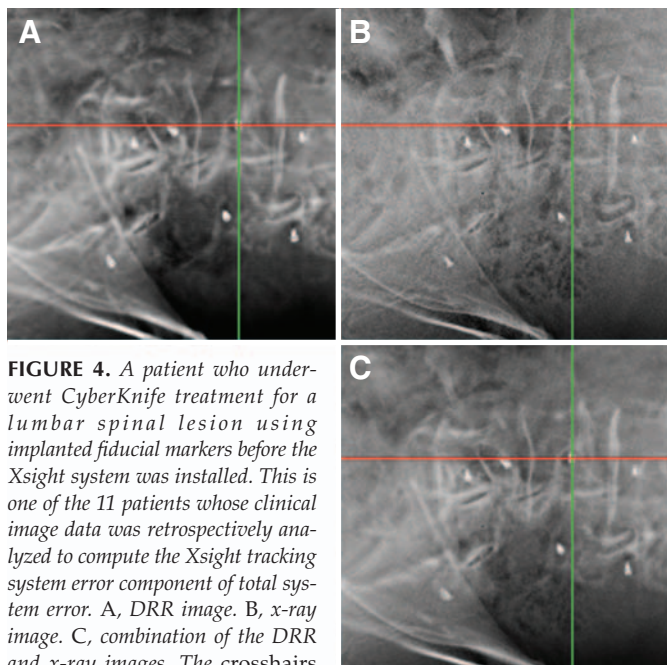


FIGURE 4. A patient who underwent CyberKnife treatment for a lumbar spinal lesion using implanted fiducial markers before the Xsight system was installed. This is one of the 11 patients whose clinical image data was retrospectively analyzed to compute the Xsight tracking system error component of total system error. A, DRR image. B, x-ray image. C, combination of the DRR and x-ray images. The crosshairs are linked in the different images. The crosshairs are positioned on a fiducial marker and show excellent alignment of the DRR and x-ray images. In the actual analysis, the fiducials were removed before performing the registration to avoid bias in the evaluation of Xsight tracking system error. In this figure, the fiducials were not removed to illustrate the excellent alignment.

pixel size and 16-bit intensity values. Only one randomly chosen pair of x-ray images per patient was used for the work reported in this article. 3) The camera calibration model and parameters for the two orthogonal x-ray imaging systems. 4) Positions (3D) of the four fiducial markers in the CT image. 5) Positions (2D) of the four fiducial markers in the two x-ray images.

RESULTS

Total System Error

The total system error of the CyberKnife, when using Xsight spine tracking and as measured with an anthropomorphic head-and-neck phantom containing a ball-cube film holder, is listed in Table 1. Seven tests were performed. All tests used the same CT scan, but had separate treatment plans. The individual total system error measurements ranged from 0.29 to 1.04 mm. The average total system error was 0.61 ± 0.27 mm (mean \pm standard deviation).

Tracking System Error

The target registration error, which represents only the Xsight tracking error component of total system error, as computed from clinical image data obtained from patients with implanted markers, is summarized in Table 2. Each of the 11 patients had four implanted fiducials, thus there are 44 individual error measurements. The individual error measure-

TABLE 1. Total system error of the CyberKnife radiosurgery system using Xsight spine tracking measured by using an anthropomorphic head-and-neck phantom and a ball-cube film holder, including the components of error along the three coordinate axes^a

Measurement no.	Error components (mm)			Total system error (mm)
	I/S	L/R	A/P	
1	-0.20	0.31	-0.08	0.38
2	-0.06	0.28	-0.04	0.29
3	-0.24	0.37	-0.06	0.45
4	-0.27	0.17	-0.42	0.53
5	0.03	0.37	0.73	0.82
6	0.31	0.32	0.94	1.04
7	-0.07	0.41	0.66	0.78
Mean				0.61
SD				0.27

^a I/S, inferior/superior; L/R, left/right; A/P, anterior/posterior; SD, standard deviation.

ments ranged from 0.14 to 1.00 mm. The average Xsight tracking system error was 0.49 ± 0.22 mm.

DISCUSSION

Lars Leksell is often quoted to have said, "Tools used by the surgeon must be adapted to the task, and where the human brain is concerned, no tool can be too refined." Given the delicate nature of the spinal cord, much the same could and should be said about stereotactic instrumentation used for treatment of spinal disorders, especially radiosurgical systems. However, what constitutes a "refined tool"? We would argue that in the case of stereotactic instrumentation, geometric targeting accuracy is a critical determinant of whether or not a clinical treatment application can be safely pursued. It is with this concern in mind that the present study was conducted.

The purpose of the present study was to assess the accuracy of the Xsight spine tracking system. The goal of any stereotactic radiosurgical equipment is to precisely deliver the planned dose distribution. The total system error for such an instrument is the geometric error in the delivery of the planned dose distribution. Because it is generally not possible to place a dosimeter in a patient's body, the total system accuracy of a radiosurgical device is best estimated using phantoms that mimic patient treatment with relatively realistic anatomy from the perspective of CT and x-ray imaging and radiation dosimetry. Thus, in this study, the total system error was measured using a realistic anthropomorphic head-and-neck phantom. The total system error (the distance between the centroids of the planned and delivered dose distributions) represents all possible errors in the treatment planning and delivery process, including error in the tracking system, the CT scanner, the treatment planning software, the robot, and the linear accelerator.

TABLE 2. Target registration error, which is the Xsight tracking system error component of total system error, computed from clinical image data obtained from 11 patients who underwent CyberKnife treatment for spinal lesions using implanted fiducial markers^a

Patient no.	Spinal region	Target registration error (mm)				Patient mean
		Target 1	Target 2	Target 3	Target 4	
1	Cervical	0.55	0.96	0.36	0.50	0.59
2	Cervical	0.61	0.34	0.77	0.21	0.48
3	Cervical	0.45	0.47	0.58	0.29	0.45
4	Cervical	0.79	0.83	0.33	0.44	0.60
5	Thoracic	0.49	0.32	0.42	0.39	0.41
6	Thoracic	0.62	0.41	0.27	0.21	0.38
7	Thoracic	0.68	0.60	0.92	0.70	0.73
8	Lumbar	0.50	0.31	0.14	0.16	0.28
9	Lumbar	0.24	0.24	0.60	0.63	0.43
10	Lumbar	0.46	0.24	0.37	0.48	0.39
11	Lumbar	0.25	0.76	0.61	1.00	0.66
Mean						0.49
SD						0.22

^a SD, standard deviation. The mean and SD were computed over the 44 individual target registration errors.

The total system error of the CyberKnife Xsight spine tracking system was measured in this study to be 0.61 ± 0.27 mm. In a previous analysis of CyberKnife cranial tracking accuracy, the total system error was measured to be 1.1 ± 0.3 mm (5) and a previous analysis of CyberKnife fiducial-based tracking accuracy in the spine found a total system error of 0.7 ± 0.3 mm (38). Consequently, the total system error of the Xsight spine tracking system is comparable to, and, in fact, slightly less than, the previously reported total system error measurements of the CyberKnife cranial tracking and fiducial-based tracking methods.

Clinical Relevance

It is well known that measurements in phantoms generally underestimate the actual application accuracy in the clinical environment. With the CyberKnife concept, the component of total system error that is likely to differ most between the experimental and clinical situations is the tracking system error. To assess the extent of this inaccuracy, the current study sought to isolate the tracking system error in a realistic clinical situation. This goal was met by retrospectively analyzing clinical image data from 11 patients with implanted fiducials who underwent CyberKnife radiosurgery for spinal lesions. The target registration error, which is an estimate of the tracking system error component of total system error and was computed using 44 fiducials from 11 patients, was found to be 0.49 ± 0.22 mm. This value quantifies how accurately the Xsight spine tracking system can calculate the spatial coordinates of discrete anatomic points. Although this measure does

not include the other possible errors in the treatment delivery process, it is reasonable to assume that the other errors in treatment delivery are similar in the experimental and clinical situations. If this assumption is valid, then the total system error in clinical application would be less than 1 mm. In the worst case, in which all errors measured in the phantom studies are owing to non-tracking system errors, the experimental (non-tracking) and clinical (tracking) error components add in quadrature and the clinical total system error would be 0.78 mm (square root of the sum of the squares of experimental error, 0.61 mm; clinical error, 0.49 mm).

Limitations of Current Analysis

The use of a ball target and a spherical dose distribution makes the measurement of total system error insensitive to errors in rotation around the center of the ball target. Although the tracking results presented here certainly have errors in rotation, the nature of the Xsight spine tracking algorithm makes it unlikely that these rotations are around the ball target center. The measurement of total system error in this study is sensitive to errors in rotation not around the center of the ball target. Also, the Xsight tracking system error measurements are inherently sensitive to errors in rotation. The Xsight system computes the position (three translations) and orientation (three rotation angles) of the skeletal anatomy in the treatment room coordinate system. The target registration error (tracking system error) was computed for each target as the Euclidean distance between the 3D position of the marker in the treatment room coordinate space computed by backprojecting its 2D positions in the x-ray images; its 3D position was determined using the six degree-of-freedom rigid transformation resulting from the 2D-3D registration (tracking). Errors in the orientation (rotation angles) of the skeletal anatomy will be reflected in this measure of registration error because errors in rotation will change the 3D position determined by the Xsight tracking software. An implanted fiducial marker is appropriate as a reference for computing registration error (tracking system error) because its localized 2D positions in the x-ray images and backprojected 3D position in the treatment room coordinate space have relatively small error (approximately 0.2–0.3 mm).

The measurements in this study can be applied strictly only if there is no patient movement. Total system error was determined by delivering radiation to a static phantom and reflects only the error present at the instant the patient’s x-ray images were acquired. Experience demonstrates that during the course of treatment, multiple small changes in a conscious patient’s position are common, regardless of the extent of immobilization. Murphy et al. (28) examined patterns of patient movement during frameless image-guided radiosurgery. They observed systematic long-term changes in position, which can be compensated for only by periodic monitoring of the target position during treatment. Short-term (1–5 min) movement of the spine averaged approximately 0.5 mm in each direction. They concluded that a tracking system that can measure the target position once per minute during a 30-minute treatment

fraction will allow less than 2% of the dose to be off-target by more than 2 mm. This means that for the Xsight spine tracking method to be practically useful, it needs to be relatively fast. The current tracking algorithm is implemented on a PC workstation with dual Intel Xeon 3.0 GHz processors. With this computer configuration, the computation time for the tracking process is approximately 2 to 3 seconds for each pair of acquired digital x-rays.

Comparison with Fiducial-based Targeting

Fiducial-based targeting methods are, in general, fast, accurate, and robust (26, 38). Algorithms for localizing implanted markers visible in x-ray images are independent of anatomy and readily automated. Software identification can also take advantage of the marker's shape and size to more accurately compute a point in space. Three non-collinear markers are mathematically required to determine the position and orientation of a stereotactic target. We commonly used additional markers to increase accuracy and provide redundancy in the event that a fiducial migrated, e.g., as a result of poor bony purchase or was not visible in the x-ray image, e.g., was obscured by adjacent dense bone.

Despite its technical simplicity and generally good performance, fiducial-based tracking for radiosurgery has numerous drawbacks. The primary shortcoming is that an initial operation, albeit minor, is required. As a result, surgical implantation is both modestly painful and harbors the potential for complications (33). Because of the intrinsic mobility, relatively small size, and fragility of the vertebral elements, the risks associated with fiducial placement are of special concern for the cervical spine; the depth of muscle and fascia in the neck also results in increased postoperative pain when fiducials are placed in this region. Furthermore, despite the simplicity of fiducial insertion, there are technical nuances that, if not followed correctly, can result in fiducial migration (with respect to the target) or inadequate x-ray visualization. In addition, permanently implanted fiducials can produce imaging artifacts that interfere with the interpretation of posttreatment CT and magnetic resonance imaging scans. Moreover, a two-step process makes fiducial-based CyberKnife radiosurgery considerably more time consuming and complex than cranial CyberKnife radiosurgery and can greatly complicate patient scheduling. Finally, the time, resources, and economic costs associated with surgical insertion of fiducials are not inconsequential. At our institution, charges for the fiducial implantation procedure exceed \$10,000. By obviating the need for implanted markers, the Xsight tracking system eliminates these problems, which are intrinsic to any fiducial-based targeting scheme.

Qualitative Impression

During the 3 years preceding the installation of the Xsight spine tracking software on the CyberKnife system at Stanford University Medical Center (September 2004), 75 spinal patients underwent radiosurgery with fiducial-based tracking. Between the time Xsight was installed and December 31, 2005,

82 patients with 94 spinal lesions underwent CyberKnife radiosurgery at our institution. It is worth noting that in the 3 years preceding the availability of Xsight, the Stanford CyberKnife treated an average 25 patients per year. In the 15 months since this software became available and made spinal radiosurgery so much more convenient, our facility averaged 66 patients per year. Because the number of radiosurgical sessions per lesion in this experience ranged from one to five (one session, 21 lesions; two sessions, 31 lesions; three sessions, 24 lesions; four sessions, three lesions; and five sessions, eight lesions), the total number of discrete radiosurgical treatments was 207. Xsight spine tracking was used and appeared adequate in every one of these patients. Of particular note, this was also true for several patients in whom there were implanted surgical clips and the eight patients who had spinal instrumentation at the affected levels. An example of such a patient with a three-level fusion and anterior cervical plating treated by the CyberKnife is shown in *Figure 5*.

The spinal pathologies treated at Stanford include metastatic disease (including prostate, breast, lung, renal, and colorectal cancer sources), benign and malignant primary spine tumors (including schwannoma, meningioma, neurofibroma, ependymoma, hemangioblastoma, and hemangiopericytoma), and vascular lesions (arteriovenous malformations and a carotid body tumor). In the case of one intramedullary hemangioblastoma, the target diameter was a mere 8 mm, thereby mandating the highest measure of radiosurgical precision. The lesions ablated with radiosurgery using Xsight ranged throughout the spinal axis including the cervical (24 lesions), cervical-thoracic (3), thoracic (37), thoracic-lumbar (2), lumbar (23), lumbar-sacral (2), and sacral (3) spine. Multiple lesions in individual

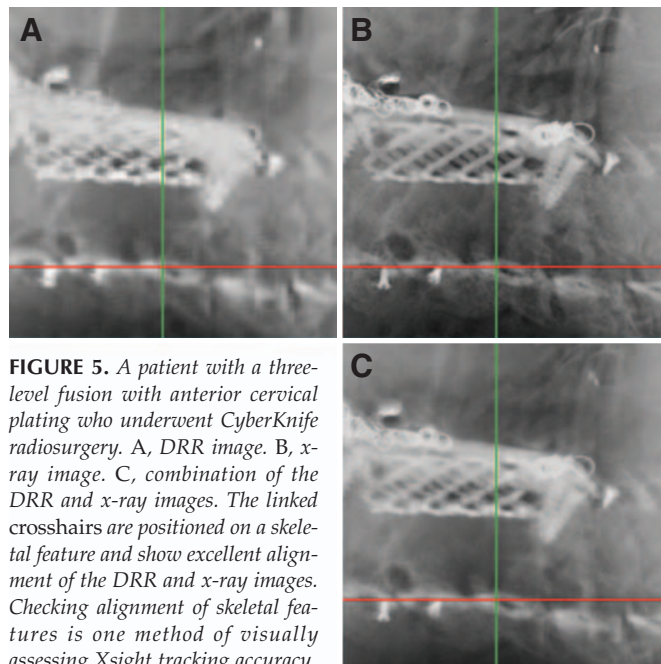


FIGURE 5. A patient with a three-level fusion with anterior cervical plating who underwent CyberKnife radiosurgery. A, DRR image. B, x-ray image. C, combination of the DRR and x-ray images. The linked crosshairs are positioned on a skeletal feature and show excellent alignment of the DRR and x-ray images. Checking alignment of skeletal features is one method of visually assessing Xsight tracking accuracy.

patients were readily accommodated by defining treatment plans for each lesion; the advantage of eliminating implanted fiducials was especially apparent in this group of patients.

Despite the practical utility of the Xsight tracking system and the fact that targeting is heavily automated, it is important to emphasize the key role of the surgeon and other users in ensuring the safety of CyberKnife radiosurgery for spinal lesions. Continuous visual inspection and monitoring are necessary because, occasionally, the Xsight tracking algorithm can report a grossly inaccurate target position. In our experience to date, this occurred twice, both times during initial alignment with heavyset patients. The algorithm has more trouble with large misalignment, which can occur during initial patient setup. In these two cases, the issue was compounded by poor contrast owing to the large size of the patient. Fortunately, such errors are readily recognized by a knowledgeable user and easily addressed (e.g., visual inspection of grid alignment and visual inspection of image artifacts in the combined image [Fig. 2], visual inspection of skeletal feature alignment with linked crosshairs [Fig. 5]). After pausing treatment, new x-rays are acquired, a new target position is computed, and radiosurgical treatment can then be quickly resumed.

CONCLUSION

By eliminating the need for implanted fiducials, Xsight tracking greatly simplifies the process of performing spinal radiosurgery. The total system error of CyberKnife radiosurgery with Xsight tracking was measured to be less than 1 mm. Experience has shown this technology to be effective and robust under a wide range of clinical circumstances.

Disclosure

Dongshan Fu, Ph.D. and Calvin R. Maurer, Jr., Ph.D. are employees of Accuray, Inc. John R. Adler, Jr., M.D. is a shareholder and member of the board of directors of Accuray, Inc. The other authors have no personal financial interest in Accuray, Inc. or the CyberKnife radiosurgery system and have received no financial support in conjunction with the generation of this article.

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COMMENT

The concept of image-guided radiotherapy and, by extension, image-guided radiosurgery has achieved paramount importance in the radiation delivery marketplace. Two basic concepts are currently being used for such treatments.

The first group of devices are those that use orthogonal x-ray imaging, such as the Cyberknife (Accuray, Sunnyvale, CA) or stereoscopic x-ray imaging, in conjunction with optical tracking such as the Novalis Exactrac 6D device (BrainLAB, Heimstetten, Germany). These devices precompute digital reconstructed radiographs based on pretreatment volumetrically reconstructed planar images and then compare them with orthogonally arranged active portal images. High performance computers then compare these digital reconstructed radiographs to the port images and make corrections to beam positioning or patient positioning to ensure accurate delivery of radiation.

The second solution involves the use of on-board imaging systems using some form of computed tomography such as the Trilogy (Varian Medical Systems, Palo Alto, CA), Synergy (Elekta AB, Stockholm, Sweden), and Hi-Art (Tomotherapy, Madison, WI) devices. These devices allow for volumetric imaging and rapid registration or planning to be performed on the treatment table at the time of patient positioning.

All of these devices and their various implementations seem to work well, at least for bony structures, without the need for implanted fiducial markers. The advantage of on-board computed tomographic imaging is the ability to localize not only bony landmarks but also soft tissue structures on the treatment table. In addition, on-board imaging solutions can allow for adaptive image-guided radiotherapy, i.e., modifying the treatment plan interfractionally to account for early tumor response to radiotherapy or tumor movement. Such changes in relative tumor movement and size are particularly relevant when treating soft tissue tumors such as those found in the prostate, lungs, and liver.

However, for the tracking of bony structures such as the spine, both strategies would seem to work equally well.

The technology discussed in this article involves Accuray's implementation of spine tracking without the use of implanted fiducials. This solution seems to work well in the hands of the developers of the technology with small errors in the present phantom study. As such, many consider it a viable alternative to image-guided radiotherapy and image-guided radiosurgery of the spine.

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The newly introduced Xsight Spine Tracking System (Accuray, Inc.) for use in the CyberKnife stereotactic radiosurgical procedure relies on the bony anatomy of the spine to automatically locate and track lesions along the spinal column. The technique marks a major advance in noninvasive spinal stereotactic radiosurgery. The system eliminates the need for surgical implantation of uncomfortable radiographic fiducials and, as a result, enables clinicians to treat spinal radiosurgical lesions easily without numerous fiducial-related drawbacks such as the invasive method of the procedure, waiting period, extra cost, and imaging artifacts that interfere with the interpretation of posttreatment computed tomography and magnetic resonance imaging scans. Because of the close proximity to the spinal cord, the accuracy of radiation beam targeting directly affects the outcome of patient treatment.

In their phantom study, Ho et al. measured an average total system error of 0.61 ± 0.27 mm based on one set of computed tomographic scans using the Xsight Spine Tracking System. However, the cause of relatively large deviations (range, -0.42 – 0.94 mm) in the anteroposterior direction was unexplained. In their retrospective study, they reported an average tracking system error component of 0.49 ± 0.22 mm. Unfortunately, only one randomly chosen pair of x-ray images per patient was used for analysis. I strongly believe all x-ray images for each patient should be examined to demonstrate the robustness of the Xsight tracking algorithm and to compare Xsight tracking with the fiducial tracking.

A number of issues should be emphasized for CyberKnife stereotactic radiosurgery using the Xsight Spine Tracking System. First, as authors point out, continuous visual inspection and monitoring are necessary because the Xsight software can sometimes report a grossly inaccurate target position. In addition, the tracking algorithm is sensitive to errors in rotation. We have often experienced inaccurate rotation errors reported by the Xsight software. Finally, the importance of accuracy of radiation targeting cannot be overestimated. During a routine quality assurance check at our institute, the total system error was found to be about 3 mm, which greatly exceeds the manufacturer's specification of less than 1 mm. The accuracy was reconfirmed within the specification by end-to-end tests after several adjustments, including robot remastering and secondary calibration of the treatment paths. The likely causes suggested by the manufacturer were not very convincing. By nature, any mechanical system can fail at any time. Failure to identify the true cause of the problem could result in its happening again at any time regardless of how often quality assurance is performed, and this could potentially expose patients to great risks.

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