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Original article

Fiducial-free real-time image-guided robotic radiosurgery for tumors of the sacrum/pelvis

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ABSTRACT

Background and purpose: Radiosurgery is a non-invasive treatment for many spinal tumors. Sacral radiosurgery, however, requires invasive fiducial marker insertion to target and track the tumor's position. We present preliminary clinical results and phantom accuracy measurements of sacral radiosurgery using fiducial-free alignment based on vertebral anatomy distant to tumor location.

Materials and methods: Fifty-one lesions in 38 patients were treated using fiducial-free spinal tracking of the L5 vertebra. An anthropomorphic phantom was used for accuracy measurements of this approach. Dose planning was based on 1.0 mm computer tomography slices using inverse treatment planning.

Results: Tracked targets were up to 17 cm from the treated tumor. Phantom tests produced an overall mean targeting error of 1.43 mm (± 0.47 mm). Patient median follow-up was 12.7 months. Local tumor control was 95%. Treatment doses were 12–25 Gy with a median prescription isodose of 65% (40–70%) and tumor volumes between 1.3 and 152.8 cc. No short-term adverse events were noted during the follow-up period.

Conclusions: Fiducial-free tracking of the lower lumbar vertebrae is a feasible, accurate, and reliable tool for radiosurgery of sacral and pelvic tumors. It is a valuable novel alternative to surgical procedures and conventional fractionated radiation therapy for these challenging cases.

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Treatment of tumors of the sacrum and pelvic ring represents one of the most difficult problems in musculo-skeletal oncology [1]. The intricate anatomy and multiple biomechanical functions within the sacral region make surgical treatment of sacral tumors complex. Massive blood loss combined with loss of neurological, bowel and bladder function are common complications of sacral tumor resections. As a result, surgical treatments are associated with considerable morbidity and can impact overall quality of life. Furthermore, the lack of precision of conventional external beam radiation and the limitations of target immobilization techniques have precluded the delivery of large doses of radiation to this area.

Spinal radiosurgery is a relatively new method for primary or adjuvant treatment of spinal tumors [2–4]. Several reports have described its accuracy and clinical effectiveness in selected patients, mainly with solitary lesions of small volume [5–7]. Tumor

tracking has been accomplished using fiducials implanted in bones close to the target lesion [3–5,8]. Fiducial placement is an invasive, and potentially painful, procedure whereby small screws are attached to the sacrum and/or pelvic ring. Fiducial implantation introduces an invasive component to an otherwise non-invasive treatment and fiducials might migrate between the implantation date and the actual treatment date. Manufactures of gantry-based treatment modalities added imaging components (kV imaging, MV imaging and cone beam CT) for an image-guided setup of the patient prior to every treatment fraction to reduce the setup error inherent to conventional radiation therapy. During the setup 2D images or 3D datasets were compared and translational offsets corrected by moving the treatment couch. During the treatment patient position is not monitored and thus there is no tracking of patient motion after the setup phase of the treatment [9,10].

Recently a new tracking algorithm for fiducial-free tracking of spine lesions (skeletal structure tumor tracking of the vertebrae) has been introduced for the Cyberknife® system to make spinal radiosurgery a completely non-invasive treatment approach [7,11]. This procedure is effective for tumors in most of the spine, as long as bony information is available from vertebrae close to the target lesion. The current skeletal structure tracking algorithm is

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specifically developed for Cyberknife treatment. This algorithm is limited to tracking vertebral bodies and not the pelvic crest and other abdominal/pelvic bony landmarks. It would be ideal if the fiducial-free tracking method of the spine was also possible for non-invasive radiosurgery of lower sacral/pelvic lesions, however, the distance between the nearest vertebral bodies and the target lesion is frequently larger than typically considered approachable for fiducial-free tracking of spinal lesions. Therefore, in the current study we ask whether the methodology of fiducial-free tracking to the lower spine could also be used for radiosurgical treatment of tumors of the sacral bone and the pelvic ring. We here report for the first time on the tracking system's clinical feasibility and targeting accuracy for image-guided robotic radiosurgical treatment of tumors of the sacrum and the pelvic ring.

Methods

Robotic radiosurgery

The Cyberknife[®] robotic radiosurgery system (Accuray Incorporated, Sunnyvale, CA, USA) consists of a 6-MV compact linear accelerator (LINAC) mounted on a computer-controlled six-axis robotic manipulator [2,12–15]. Integral to the system are orthogonally positioned X-ray cameras which acquire images during treatment. The images are processed automatically to identify radiographic features and registered to the treatment planning study to measure the position of the treatment site in real time [16]. The system adapts to changes in patient position during treatment by acquiring targeting images repeatedly and then adjusting the direction of the treatment beam. In contrast to a gantry-mounted LINAC, the treatment beam can be directed at the target from nearly anywhere around the patient, limited only by obstacles such as the treatment couch.

Fiducial-free spinal tracking

Image-guided radiation therapy relies on the dependable identification of landmarks – implanted fiducials or unique bony structures – on reference radiographs and live X-ray images [17,18]. The Cyberknife[®] system automatically acquires orthogonal images for the initial patient setup and between the individual treatment beams. These images are used to assess and correct for changes in position for the entire treatment session. The ortho-

nal images are referenced with digitally reconstructed radiographs (DRRs) derived from a high quality computed tomography (CT) which is also used for treatment planning. The DRRs are based on a selected reference point (CT-center) and take into account the imaging geometry of the Cyberknife[®] treatment room.

As the quality of the reference DRRs and hence the precision of the target localization depends on the CT slice spacing our scanning protocol specifies a slice thickness of 1.0 mm [19].

A perfect setup on the treatment couch would exactly reproduce the patients position on the CT scanner regarding all translations and rotations. During setup and treatment the patient is lying flat on his back in a reproducible position as during the planning CT scan. Parts of the pelvic bones (iliac bone) are seen in addition to the lower vertebrae on the DRRs and can therefore be visually correlated to the in-room acquired orthogonal imaging. This patient setup allows for a very accurate initial patient positioning. Deviations are determined by matching the reference DRRs to the live X-ray images, resulting in translational and rotational offsets. In the setup phase the deviations are minimized by 6D-movements of the treatment couch. During treatment these offset values are used by the robot to adjust the geometry of the current treatment beam to compensate in real time for intra-fractional patient shifts in position [20,21] (Fig. 1).

The safety and effectiveness of fiducial-based targeting (or, in high cervical cases, targeting based on cranial anatomy) and fiducial-free spinal tracking for Cyberknife[®] radiosurgery treatment of the spine has been previously reported [7,11].

Tracking of distant targets

The periodic tracking and compensating for patient movement by referencing unique bony anatomy in vertebrae during treatment and the high precision dose application (with a targeting error less than 0.5 mm) allows for very conformal treatment planning without using a setup margin for targets which contain or are very close to the CT-center. Because the pelvic region does not offer the unique anatomic structure required for reliable referencing, the closest region suitable for reliable tracking is the lower lumbar spine. This setup involves radial distances between the CT-center and the treatment center of up to 17 cm. Placing the treatment center this far from the CT-center could degrade targeting accuracy. Thus, tracking accuracy for sacral/pelvic targets distant from the CT-center was assessed experimentally.

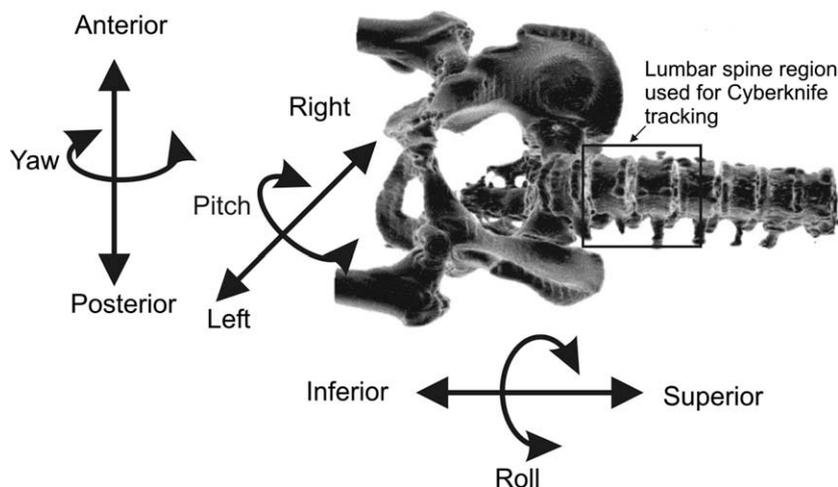


Fig. 1. Definition of the translational directions and the axis for rotational corrections. During patient setup only the 'yaw' correction has to be manually performed by rotating the patient on the couch. In the treatment phase all necessary corrections as determined by the image guidance are applied automatically. Tracking of the pelvic lesions used unique bony structures of lower lumbar spine vertebra. For our purposes, the pelvic bone and the portion of the lower lumbar spine is considered a rigid body.

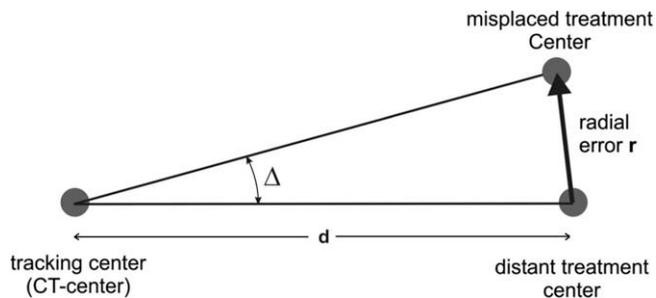


Fig. 2. The introduction of an error in the angular estimate results in a misplacement of the treatment center for the affected radiation beams. The radial error, r , is a function of the distance, d , between the tracking center (CT-center) and the treatment center.

Theoretical considerations

Patient position correction is performed for the three translational directions (superior–inferior, left–right, and anterior–posterior) as well as for the three rotational axes (roll, pitch, and yaw). Based on pure geometric considerations the error in the translational components is not affected by the distance between the CT-center and treatment center, but errors in the rotational estimates are amplified (Fig. 2). The radial displacement is a function of the error in the rotational correction and the distance between the CT-center and the treatment center. Thus, for targets where the CT-center is close to or within the target region, even a large error (1°) results in a misplacement that does not exceed 0.5 mm. For distant targets, however, a radial error of up to 2 mm can be obtained for angular errors that can realistically be anticipated (maximum values $\pm 0.5^\circ$) (Fig. 3). For the cases treated to date at our center, a distance of 170 mm was never exceeded.

The range of the rotational error was established experimentally by analyzing measured angular displacements of a series of images obtained from an anthropomorphic phantom that includes a section of cervical spine. The measurements consisted of a wide range of combinations between translational and rotational displacements encountered during real patient treatments (translational offset < 3 mm and rotational offset $< 1^\circ$) and comparing the nominal position and rotational motion with values measured

by the imaging system. The largest error in this idealistic setup was determined for roll angular estimates to be $0.3 \pm 0.1^\circ$ (1 standard deviation).

Additionally our tracking log files acquired during 250 spinal patient treatments were analyzed and grouped by the treated spinal section. For each imaging event deviations in patient position and orientation from the reference pose were recorded. These values constitute a combination of real patient movement and the statistical uncertainty of the image registration. The patient logs reveal similar translational mean shifts for all sections of the spine (~ 0.3 mm) from one imaging to the next, whereas mean roll shifts are lowest for treatments using the lower lumbar spine as the tracking target ($0.35 \pm 0.03^\circ$). Lower shifts are an indication for less motion or a lower statistical error in the tracking readouts, which both result in more accuracy for treatment delivery. Assuming that the rigid skeletal image registration accuracy along the entire spine is in fact consistent (which is supported by ground truth validation measurements [18]), the reduced movement at the lumbar spine that we have observed in our treatment records will further improve the intra-fraction targeting precision. Thus, we consider a maximum error of $\pm 0.5^\circ$ in the angular estimate to be a realistic assumption.

We base our estimates of lumbar targeting accuracy on the measurements made with the cervical spine phantom. All other things being equal (e.g., CT slice thickness, image resolution, radiograph contrast, bony edge clarity, etc.), the accuracy of translational measurements for the cervical and lumbar spine will be comparable, while rotational measurements of the lumbar spine will generally be a little more accurate than for the cervical spine, owing to the larger size of the lumbar vertebrae.

Phantom study

To simulate the clinical situation an anthropomorphic head phantom was scanned ‘feet first’ to provide the primary planning dataset for this rigid body scenario. The cervical spine section of this phantom was used to define the CT-center. The skull provides an insert which accommodates a precisely aligned orthogonal set of Gafchromic Film (International Speciality Products ISP, Wayne, NJ) and an acrylic ball which served as the target lesion. The distance between the tracking center and the treatment isocenter

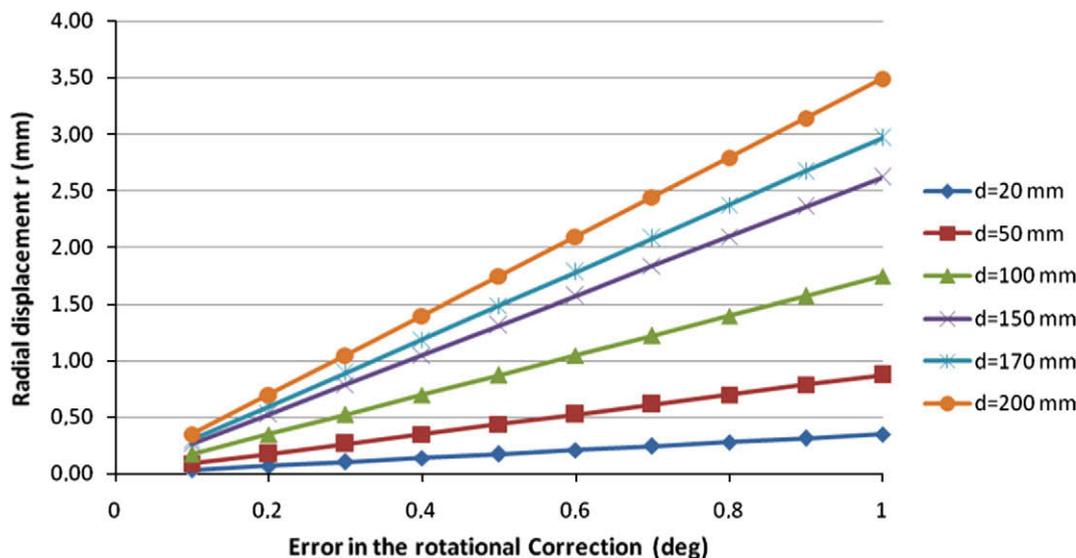


Fig. 3. Visualization of the relationship between rotational error and the resulting radial displacement, r , for selected values of the distance, d , between the tracking and targeting centers. For targets close to the tracking center, even large errors (1°) in the rotational estimate will not result in a targeting error exceeding 0.5 mm. Larger values of d require application of an appropriate margin (2 mm) to account for the radial displacements.

Table 1

A series of 6 independent phantom tests were performed. For the first 3 tests, the phantom was positioned as close to a perfect setup as possible to establish a baseline. The following tests simulated extreme combinations of offsets within the possible range of automatic online corrections.

Test	Translations			Rotations		
	Left–right [mm]	Anterior–posterior [mm]	Inf–superior [mm]	Pitch (°)	Roll (°)	Yaw (°)
1	<0.2	<0.2	<0.2	<0.1	<0.1	0.3
2	<0.2	<0.2	<0.2	<0.1	<0.1	0.1
3	<0.2	<0.2	<0.2	<0.1	<0.1	0.0
4	Right 9.4	Post. 9.4	Inf. 9.9	<0.3	<0.3	<0.3
5	<0.4	<0.4	<0.4	0.0	0.0	2.9
6	Left 9.3	Post. 9.2	Inf. 9.8	0.9	0.8	2.9

was 170 mm, which is about the largest distance that can be achieved in clinical situations. An isocentric treatment plan, yielding an almost spherical dose distribution, was designed with the Multiplan Treatment Planning System (Accuray, Inc, Sunnyvale, CA). The same plan was delivered to the phantom three times using an almost perfect setup to establish a baseline. In the subsequent tests, couch correction values were increased (Table 1) within a range where the Cyberknife® robot can correct for offsets without moving the treatment couch (translations ± 10 mm, pitch and roll rotation $\pm 1^\circ$, yaw rotation 3°).

The films were analyzed by comparing the planned and the delivered dose yielding the total system accuracy. This end-to-end test procedure (encompassing CT simulation, phantom setup, and treatment delivery) is explained in great detail by Chang et al. [20].

Patient treatment procedure

Treatment planning and delivery were performed as outpatient procedures. After consultation, the planning CT was performed with the patient placed in a supine position without vacuum bags or alpha cradles. CT images were acquired with 1 mm thick slices including the lesion as well as the L4 and L5 vertebrae. In most cases axial magnetic resonance imaging (MRI) scans of the lesion were fused with the CT for better soft tissue discrimination (T1 + gadolinium contrast). Treatment planning was performed by a specialized team of surgeons, orthopaedic surgeons and radiation physicists using the treatment planning system software Multiplan 1.4.0 (Accuray, Inc.).

Dose calculations

Tumor dose was determined on the basis of the tumor histology, nerve roots and/or cauda equina, rectum, bladder tolerance, and previous radiation. Treatment doses were equivalent to those used for cranial radiosurgery. An inverse treatment planning technique assured that the tumor received the maximum dose and placed restrictions on the maximum dose to the surrounding structures.

The possibility to deliver dose using several 100 non-coplanar, non-isocentric small beams (diameter in 80 cm distance ranging from 5 to 60 mm) enabled us to create a steep gradient towards the normal tissue. Planning goal was always to reduce the integral dose as much as possible. Bladder, rectum and, where applicable, the intestines were contoured in the planning image sets for analysis of the dose–volume histograms (DVHs) for a subset of patients. The contours covered the complete volume and not just the walls of those organs. From the DVH the following parameters were determined: maximum dose D_{\max} and the structure volume receiving a dose larger than 2.5 Gy ($V_{2.5\text{Gy}}$). D_{\max} is defined according to ICRU Report 50 and is considering dose to a clinical relevant volume exceeding 5 cm³. Deviating from the Report 50 definition of D_{\max} , which is referring to a continuous volume, we were

tabulating the dose value corresponding to the 5 cm³ structure of the DVH. This led to an intended overestimation of D_{\max} in addition to the fact that anatomy is dynamically changing caused by bladder and rectum filling as well as peristaltic movements of the intestines and the rectum contributing to a further reduction of D_{\max} to a specific organ. $V_{2.5\text{Gy}}$ was chosen because 2.5 Gy is the most commonly used fraction dose administered to a large volume including intestines and rectum in standard adjuvant radiation treatments of the pelvic region.

Because the beam directions are not confined to a common isocenter, the system can produce complex dose distributions. All treatments were performed in a single fraction. Patients were positioned on the treatment table without any immobilization device. Pillows for patient comfort were used as they had been during the planning CT scan. Patients with significant pain received orally administered analgesics, but no further intravenous sedation was required. Each patient returned for radiosurgery within one week of treatment planning. After treatment, clinical follow-up was performed to determine any immediate adverse effects of therapy according to the time schedule mentioned above.

Patient treatments

A series of 38 patients underwent 51 radiosurgical procedures using fiducial-free tracking from October 1st 2005 to September 17th 2007. Patients presented with a Karnofsky Performance Scale score of 50 or greater. Metastatic diseases (30 patients out of 38) had been confirmed histologically from the primary tumor site (46 malignant, 5 benign lesions). Patients were also included when they harbored recurrent lesions. Eight patients had undergone surgery of the treated site, and seven patients had previously irradiated lesions. There were 23 men and 15 women (age range: 19–85 years, mean: 60 years). Table 2 summarizes the characteristics of the treatment group and Table 3 shows tumor histologies.

The first clinical follow-up was performed one week after treatment to analyze the patient status, particularly the pain level, after radiosurgery. Clinical evaluation as well as CT and/or MRI imaging studies were done 3 and 6 months after treatment. If the patient could not come to the clinic due to physical disability, data were collected over the telephone and images via postal delivery. Each

Table 2
Patient characteristics (n = 38, lesions = 51).

Characteristic	No.
Regions treated acetabulum	9
Pubic bone	5
Iliac bone	7
Sacral bone	30
Chemotherapy	13
Previous external beam irradiation	7
Previous surgery	8
Multiple lesions treated	24

Table 3
Lesion histologies.

Tumor	No.
Metastatic lesions (Total)	46
Urogenital	24
Lung	1
Gastric intestinal	5
Sarcoma	3
Neuroendocrine carcinoma	1
Breast	9
Others	3
Benign lesions (total)	5
Ependymoma grade III	2
Neurinoma	2
Chordoma	1
Total lesions	51

evaluation included a clinical examination and a 10-point pain scale compared with pain assessed on the day of treatment. Images were analyzed for local tumor control and distant progress. Whenever possible, functional imaging such as PET or PET-CT was used to support the evaluation of tumor activity.

Results

Phantom study

None of the experimental tests revealed a total tracking error larger than 1.9 mm (Table 4). The mean tracking error was 1.4 mm. Targeting precision was mainly influenced by a rather large left–right error (mean value 0.86 mm) compared to the other components contributing (superior–inferior error: mean value 0.17 mm and anterior–posterior error: mean value 0.21 mm).

The largest error was found in the series of 3 tests where the setup error was minimized and thus the X-ray image geometry reflected the DRR geometry. None of the analyzed parameters showed a trend corresponding to the magnitude of the offset or if a rotational component was present. The test results showed no dependency on the introduced setup error.

Table 4

Phantom test results referring to the setup parameters are described in Table 1. The 2 orthogonal films are scanned following which their profiles are analyzed and compared with the planned dose distribution. This yields a left–right and an anterior–posterior error for the axial film; and a superior–inferior and a second anterior–posterior error for the sagittal film. Thus, the total targeting error describes the radial distance between the centroid of the planned dose distribution and the finally delivered dose. There is no obvious relationship between the targeting error and the chosen offsets.

Test	Left–right error [mm]	Superior–inferior error [mm]	Average anterior–posterior error [mm]	Total targeting error [mm]
Optimal setup (1)	–1.79	–0.43	–0.23	1.85
Optimal setup (2)	–1.51	–0.29	–0.20	1.55
Optimal setup (3)	1.59	–0.09	–0.31	1.62
Max translations (4)	–1.17	–0.18	–0.37	1.24
Max yaw (5)	–1.76	0.04	–0.01	1.76
Max offset (6)	–0.55	–0.08	–0.12	0.56
Mean	–0.86	–0.17	–0.21	1.43
Standard deviation	1.29	0.17	0.13	0.47

Patient data

Fifty-one pelvic lesions were treated in 38 patients. The tumor volume ranged from 1.9 to 104.3 cc (mean: 25 cc). Eight patients were treated after previous surgery, 3 because tumor resection was incomplete, and 5 because follow-up imaging revealed tumor progression at the site of resection. Repeat surgery was declined either by the referring surgeon or by the patient. Seven lesions

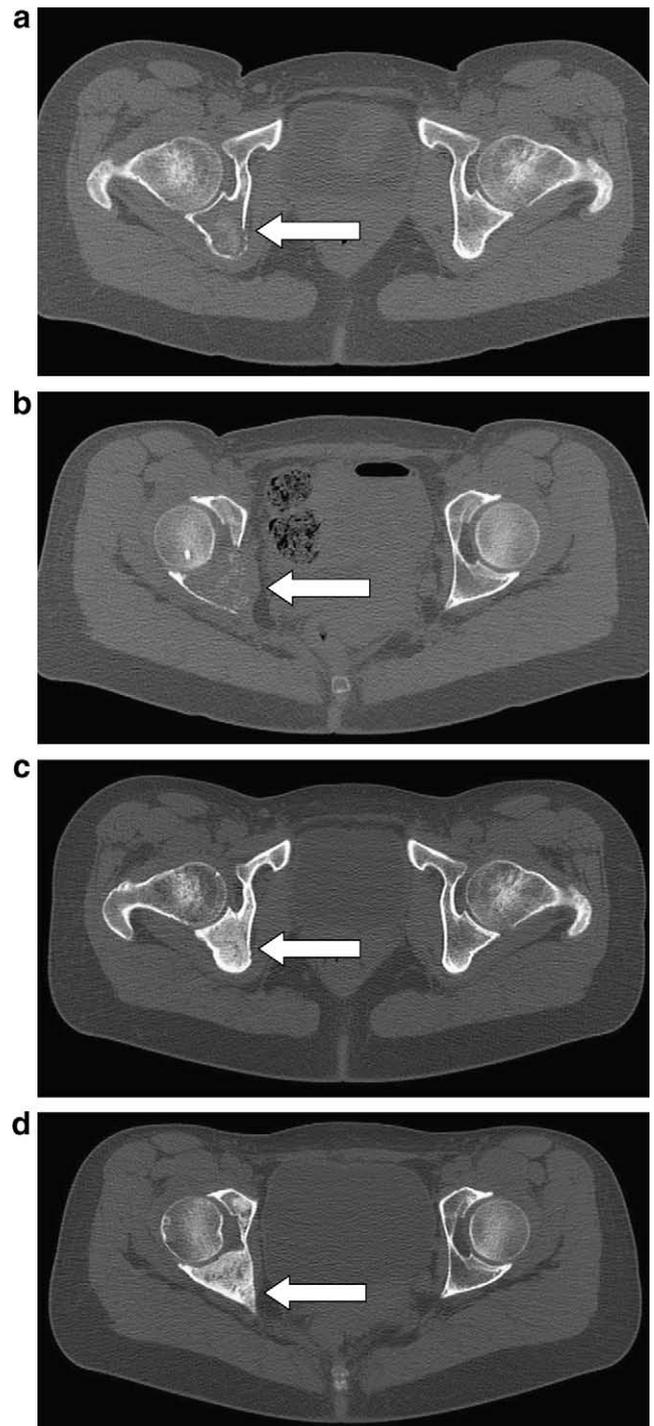


Fig. 4. (a and b) A metastasis in the dorsal part of the right acetabulum of a 55-year-old renal cell cancer patient. Single-fraction Cyberknife® treatment with 20 Gy was performed as an alternative to surgery and conventional fractionated radiotherapy. (c and d) A complete re-ossification of the irradiated bony structures 6 months after treatment.

had received previous external beam irradiation; in these patients additional conventional irradiation was precluded due to previous doses. Thirteen of the 38 patients treated in this study received additional systemic therapy. Follow-up ranged from 8 weeks to 35 months with a mean follow-up of 12.7 months.

The local tumor control was 95%. One patient, with a large sacral chordoma, experienced a local recurrence as defined by PET scanning and biopsy. He underwent subsequent surgery and repeated radiosurgery for unresectable tumor parts. Another patient, with a presacral metastasis, developed a tumor recurrence from the border of the treated lesion with an invasion into the sacral foramina of the second and third sacral nerve roots. She was treated again at the level of the osseous foramina for pain reduction.

All tumors were treated in a single fraction of 13.5–24 Gy (mean 19.4 Gy) to a mean isodose line of 67% (40–80%). The fiducial-free tracking procedure was effective in all cases, even without patient-immobilization devices (Fig. 4). Setup time for patient alignment on the treatment couch averaged 6 minutes (range: 2–18 min). A mean of 149 beams (54–382) were applied, which corresponds to a median treatment time of 80 min, but with a rather large variation depending on shape, size, location, and depth of the tumor. Seventeen of 24 patients, treated for pain related to their lesion as the primary indication for radiosurgery, experienced a significant pain reduction during the first three weeks of treatment. The pain status of the remaining 7 patients did not change. No symptoms such as radiation-induced myelopathy, hemorrhage, neurological changes, and requirement of hospitalization immediately after treatment occurred. There were also no short-term adverse events in the patient group who received conventional fractionated radiotherapy before radiosurgery.

Dose calculation organs at risk

The results of dose delivery to organs at risk were sorted by the target location and the target volume for a relevant subset of patients and are displayed in Table 5.

Discussion

The introduction of fiducial-free spinal tracking enabled the periodic tracking of spinal lesions based on anatomical landmarks of the vertebra instead of surgically implanted fiducials. Data about technical accuracy in a clinical setting and first clinical results obtained using this new fiducial-free spinal tracking procedure with a non-rigid deformation model were presented recently documenting the accuracy and feasibility of this technology [7,11]. We hypothesized that fiducial-free tracking might also be used for non-invasive radiosurgical treatment of tumors of the pelvic bone which are distant to the tracking area. Because of the relatively fixed connection between the lower spine and the sacral/pelvic bone it was thought to be reasonable to analyze this approach in a phantom study prior to the first clinical application of this procedure.

Phantom tests

Our phantom tests showed that for distant targets an increased targeting error has to be accounted for. In the case of standard end-to-end tests where the tracking center is identical to or close to the targeting center, end-to-end tests using fiducial-free tracking resulted in a mean total clinical accuracy (total targeting error) of 0.52 mm (±0.22 mm) [7]. Factors contributing to this value are the resolution of the primary CT imaging (voxel size about 0.5 mm for a 512 × 512 pixel matrix), resolution of the Cyberknife® imaging system (about 0.4 mm), and the mechanical precision of the robot.

Table 5
Dose calculations organs at risk

Case	Tumor Location	Volume (cm ³)	Dose (Gy)	IDL (%)	Urinary bladder			Rectum			Intestine			
					Distance (cm)	Max dose (Gy)	V _{2,5Gy} (%)	Distance (cm)	Max dose (Gy)	V _{2,5Gy} (%)	Distance (cm)	Max dose (Gy)	V _{2,5Gy} (%)	
1	Os Sakrum	1.8	18	70	8.5	0.2	0	10	0.1	0	0	0.25	3	3
2	Os Sakrum	2.3	22	65	8.9	<0.1	0	5.9	<0.3	0	0	7.5	4.8	32
3	Os Sakrum	22.5	18	70	7.5	0.45	0	7	0.8	0	0	8	3.4	4
4	Os Sakrum	23.9	22	70	6.5	0.3	0	1.5	4.6	0.2	0.2	4	7.6	37
5	Os Sakrum	57.8	20	65	7.6	2.2	2	3	4.3	4	4	2.7	7.9	35
6	Os Ischii	10	20	65	7.6	3.3	9	2.7	4.8	19	19	10	2.9	6
7	Acetabulum	9.8	18	65	1.1	3.3	9	7.5	0.2	0	0	80	2.5	0
8	Acetabulum	10.6	22	65	2.6	4.1	30	4.2	4.5	29	N/A	N/A		
9	Acetabulum	16.9	18	70	1.1	6.2	26	3.1	4	9	N/A	N/A		
10	Acetabulum	23.5	18	70	6.3	0.6	0	10	0.5	0	3.8	0.9	2	0.5
11	Acetabulum	37.3	20	70	5.6	5.1	47	3	4.3	15	15	0.9	5.9	9
12	Acetabulum	70.5	18	65	1	5.5	47	1.9	3.5	28	28	0.1	7.7	45
13	Os Ilium	5.1	20	65	6.3	3.6	5	10.5	0.85	0	0	3	2.4	1
14	Os Ilium	9.7	18	65	0.15	0.15	0	7	0.1	0	0	0.9	4.4	12
15	Os Ilium	21.4	20	65	6.5	4.1	34	7	0.8	0	0	8	5.9	14
16	Os Ilium	25.4	22	70	6	1.3	0		0.65	0	0	2	5.65	12
17	Os Pubis	7.4	22	70	6	1.4	0.5	4.7	3.4	0.5	0.5	N/A		
18	Os Pubis	41.6	20	65	0.5	6.2	12	2.2	4.3	12	12			

The results achieved for distant targets in the current study correspond well with the observed uncertainties in angular estimates and the underlying model of the tracking error amplification. Even large offsets were corrected reliably by the Cyberknife® System and no additional error was introduced. Considering also that the vertebra of the lumbar spine are generally larger than the cervical spine section (height about 45 mm) of our phantom, which facilitates the recognition of an angular offset and reduces the error in the determination of the correction, a targeting error of 2 mm for clinically relevant distances should be taken into account during treatment planning for this rigid body scenario.

Dose calculation organs at risk

The results were sorted by the target location and the target volume and are displayed in Table 5. The relevant dose to surrounding critical structures is mainly influenced by the size and the location of the target. The distance between the target and the organ at risk (OAR) structure plays only a minor role if proximal structures were accounted for during the treatment planning process (see case 1 – intestine). In general: a sufficient dose to a large target requires more energy to be transported through the tissue resulting in a higher dose to OAR compared to smaller targets. Additionally the lesion size determines the size of the linac aperture; a larger size collimator is resulting in more overlapping beam volume in the entrance channels thus increasing the dose to the affected tissue by adding up the dose contributions of the individual beams.

For targets in the posterior portion of the pelvic region the elevated doses to normal tissue and the intestines are caused by beams carrying up to 250 monitor units thus depositing at the maximum of their depth dose curve approximately 2.5 Gy. For sacral bone lesions for example this can lead to maximum doses ranging from 3 to 9.9 Gy and 37% of the contoured intestines volume receiving doses exceeding 2.5 Gy even though the treatment target is far away under a radiosurgical viewpoint. In these cases the dose to bladder and rectum ($V_{2.5Gy} < 4\%$) is not beyond values obtained during a single fraction of a standard fractionated pelvic treatment.

The treatment of lesions close to the body surface (e.g., pelvic bone) is only creating negligible doses to the intestines; for other pelvic localizations the intestine $V_{2.5Gy}$ is lower than 15% of the contoured volume. Bladder and rectum doses are well below 6.5 Gy and with a $V_{2.5Gy}$ smaller than 30%.

Clinical feasibility

All radiosurgical procedures were well tolerated by our patients. Single-dose treatment was chosen because most clinical publications on spinal radiosurgery have demonstrated high efficacy and low morbidity for single fraction radiosurgery of spinal tumors [3–5,7,8,21]. A single session outpatient radiosurgical treatment is of particular value for interdisciplinary treatment of oncologic patients as it does not interfere with simultaneous systemic therapies such as chemotherapy and immunotherapy. In fact, 13 of the 39 patients treated in this study received additional systemic therapy. The stereotactic radiosurgery regime is brief and convenient for the patients.

Although follow-up is too short for conclusive clinical evaluations, the current study showed that robotic radiosurgery using fiducial-free tracking, with a tracking site to tumor distance of up to 17 cm, was feasible for tumors of the sacrum and the bony pelvis. We advocate using a planning tumor volume (PTV) with a 2-mm margin to compensate for tracking errors as found in our phantom study. This margin can be safely applied in most locations of the sacrum and pelvis as the selected cases are generally of small

volume and are not located in highly sensitive areas. The applicability of the described approach may be a unique circumstance in the human body as the lower spine – pelvic area has a relatively fixed connection when lying flat on the back. Distant tracking of bony landmarks is not advocated for other areas. Our results, therefore, should be interpreted cautiously and cannot be transferred to other areas of the body.

Treatments were performed without using an alpha cradle or other immobilization device, which is a significant advantage for patient comfort during treatment. Patients were placed in a supine position with a cushion under their legs for more comfort during CT scanning and treatment application. Keegan demonstrated that the lumbo-sacral spine is not prone to rotational movements giving further evidence that the risk of unintended and not monitored movements in this area is minimal [22].

We sought to achieve a steep dose gradient to the lesion in a single fraction. No short-term side effects were noted using this approach. In addition, eleven patients received conventional radiation 12–40 weeks before radiosurgery. None of these patients experienced radiation toxicity after radiosurgery. The median follow-up of 12.7 months implies that our analysis may underestimate the incidence of local and regional failures. A more prolonged follow-up is needed to analyze whether these preliminary favorable results will also lead to long-term local control [5]. Using all means during treatment planning to create a steep dose gradient towards the tissue surrounding the target and to avoid hot spots in the periphery, lesions in the pelvic region can be treated safely with the Cyberknife® technique.

Conclusions

Our phantom measurements and preliminary clinical data suggest that fiducial-free tracking of the lower lumbar vertebrae is a feasible, accurate, and reliable tool for radiosurgery of sacral and pelvic tumors. Fiducial implantation can be avoided which offers a new, non-invasive treatment possibility for otherwise difficult-to-treat tumors, and is therefore a valuable alternative or additional treatment option for oncological treatment concepts in selected cases. A margin of 2 mm around the border of the lesion is suggested to compensate for possible tracking inaccuracies.

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