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CORRELATION OF LOCAL FAILURE WITH MEASURES OF DOSE INSUFFICIENCY IN THE HIGH-DOSE SINGLE-FRACTION TREATMENT OF BONY METASTASES

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Abstract

Purpose—In the setting of high-dose single-fraction image-guided radiotherapy of spine metastases, the delivered dose is hypothesized to be a significant factor in local control. We investigated the dependence of local control on measures of dose insufficiency.

Methods and Materials—The minimum doses received by the hottest 100%, 98%, and 95% ($D_{\min}$, D_{98} , and D_{95}) of the gross target volume (GTV) were computed for 91 consecutively treated lesions observed in 79 patients. Prescribed doses of 18–24 Gy were delivered in a single fraction. The spinal cord and cauda equina were constrained to a maximum dose of 12–14 Gy and 16 Gy, respectively. A rank-sum test was used to assess the differences between radiographic local failure and local control.

Results—With a median follow-up of 18 months, seven local failures have occurred. The distributions of GTV $D_{\min}$, D_{98} , and D_{95} for treatments resulting in local failure were found to be statistically different from the corresponding distributions of the patient group as a whole. Taking no account of histology, p values calculated for $D_{\min}$, D_{98} , and D_{95} were 0.004, 0.012, and 0.031, respectively. No correlations between local failure and target volume or between local failure and anatomic location were found.

Conclusions—The results indicate that $D_{\min}$, D_{98} , and D_{95} may be important risk factors for local failure. No local failures in any histology were observed when $D_{\min}$ was >15 Gy, suggesting that this metric may be an important predictor of local control.

Keywords

Paraspinal metastasis; High-dose single-fraction radiotherapy; Local failure; Dose insufficiency

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INTRODUCTION

The treatment of oligometastatic disease of the spine, pelvis, and paraspinal sites using stereotactic body radiation therapy is now well established (1–7). Treatment based on stereotactic body radiation therapy is given as either a single fraction, or up to five treatments in a hypofractionated regimen.

The design of a tumoricidal distribution for some sites is greatly complicated, if not confounded, by the need to keep the dose to the spinal cord or other critical structures below tolerance. Irradiating the cord above its tolerance can result in radiation myelitis, a potentially devastating complication. Universally agreed-on dose–volume constraints on the cord dose in the setting of high-dose single-fraction treatments have not yet been established, however. A recent review of the literature has been given by Sahgal *et al.* (8). The target shapes are often complex, partially or completely wrapping the spinal canal, for example. Inverse treatment planning is used to help optimize the target dose uniformity while minimizing the dose to the critical structures. This necessitates the use of intensity modulation when a conventional C-arm treatment machine (9–10) or a tomotherapy machine (11) is used. The robotically positioned LINAC of the Cyber-knife delivers similarly optimized dose distributions using a nonisocentric technique (12). In all cases, image guidance is used to deliver the dose with high spatial accuracy, with uncertainty generally less than 2 mm (10, 13–15). An unavoidable feature that can arise when the cord is within a few millimeters of the target is that part of the target will be underdosed. The maximum dose gradient that can generally be achieved with intensity-modulated delivery has been reported to be 10% per millimeter (11, 16). Thus if, for example, the maximum point dose to the spinal cord is restricted to 14 Gy, then it will not be possible to deliver 24 Gy to that part of the target that lies within 3 mm of this point.

An actuarial local control rate of 84% at 1 year has been reported by Chang *et al.* (2) using an intensity-modulated beam delivery and image guidance using a computed tomography (CT)-on-rails system. The clinical outcomes for high-dose single-fraction treatment of bony metastases to the spine and paraspinal sites at Memorial Sloan-Kettering Cancer Center, including local control and pain control, have been reported by Yamada *et al.* (1). The overall actuarial local control rate for single-fraction treatments of bony metastases was 90% at 15 months. Importantly, a dose response was also seen. The probability of local control for patients treated to 24 Gy was 95%, compared with a probability of 80% for patients treated to between 18 Gy and 23 Gy.

Given the observed dose response, we investigated the hypothesis that underdosing to small subvolumes of the target is clinically significant. In this study, we report on correlation between radiographic local control and measures of under-dosing that arise because of the need to protect normal structures.

METHODS AND MATERIALS

This is a retrospective analysis of the planned dose distributions of 91 lesions in 79 patients who were treated consecutively between May 2003 and November 2006 and for whom dose distributions could be retrieved from the archive. All patients had metastatic disease of the spine or of the bony pelvis. Patients were excluded from single-fraction treatment if they had previously received radiotherapy to the target. Most patients were undergoing chemotherapy before treatment. They were required to temporarily suspend the chemotherapy from 1 week preceding treatment until 1 week after treatment. After treatment, all patients underwent

magnetic resonance imaging (MRI) every 3 to 4 months. These scans were examined by a neuroradiologist for evidence of failure.

Dose distributions were planned with an in-house treatment planning system using an inverse-planning optimization technique. A pencil beam convolution algorithm incorporating tissue inhomogeneity was used to calculate dose. Treatments were delivered using dynamic intensity-modulated radiotherapy. Beam arrangements were all coplanar, generally six to eight mostly posterior and posterior-oblique directions to minimize dose to abdomen or thorax. The prescription dose was between 18 and 24 Gy. The beam energy was generally 6 MV. On occasion, a 15-MV beam was used if an anterior beam was used for a deep-seated tumor in a larger patient. Treatments were delivered using a linear accelerator (Varian 2100C) equipped with a 120-leaf multi-leaf collimator with a leaf width of 0.5 cm projected to isocenter. The gross target volume (GTV), clinical target volume (CTV), planning target volume (PTV), spinal cord (extended 1.5 cm above and below the involved vertebra), and other critical structures such as the esophagus, kidneys, liver, and bowel were contoured. The dose constraints used are listed in Table 1.

In general, the CTV is taken to be the vertebral body. The PTV was created using a 0.3-cm expansion of the CTV, except where this would have included the spinal cord or esophagus. Near these critical structures, the PTV is pulled back to the CTV boundary. The PTV may include the involved vertebral body, surrounding soft tissues, the inferior region of the superior vertebra, and the superior region of the inferior vertebra. The plan is normalized such that the maximum cord dose meets the cord constraint for the particular patient. The prescription isodose line generally encloses the PTV, except in the vicinity of the spinal cord. Figure 1 is an example where the prescription isodose curve does not completely surround either the CTV or the PTV, to keep the maximum cauda dose below tolerance.

The image guidance procedure was initially based on the use of implanted markers and MV localization images. A single patient was set up using an earlier system: a CT scanner positioned in the treatment vault (17). Two gold fiducial markers were implanted into the posterior elements of the involved vertebra and the posterior elements of the superior and inferior vertebrae: six in total. Digitally composited radiographs were used for reference images instead of the more conventional digitally reconstructed radiographs. In a digitally composited radiograph, the Hounsfield numbers of the CT scan can be manipulated. The opacity of voxels with numbers corresponding to that of metal is modified in a procedure analogous to windowing and leveling (14). The effect is to increase the contrast of the implanted fiducial markers, making them visible and hence useable as fiducial markers in the image registration procedure.

After an institutional review board—approved protocol established that both the systematic and the random uncertainties of kV cone-beam image guidance were either less than or comparable to those of the technique based on the use of implanted markers and MV imaging, the use of implanted markers was discontinued, and direct cone-beam localization of the bony anatomy near the target was used to position patients. The number of treatments given using in-room CT, pairs of MV localization images and implanted markers, and cone-beam localization were 1, 55, and 35, respectively. The systematic uncertainties of MV and cone-beam—guided setups in our clinic have been studied and found to be on the order of 1.0 mm and 0.3 mm, respectively (18). The random uncertainties of registration of the markers implanted into the spine using MV images was found to be $0.5 \text{ mm} \pm 0.5 \text{ mm}$. The random uncertainties of the cone-beam CT registration were found to be less than or equal to those of the MV technique. In consequence, the combined overall uncertainty in target positioning is estimated to be less than 2 mm for both techniques (18).

Patients were immobilized in a paraspinal immobilization cradle developed specifically for these treatments. Because the treatment sessions were long, usually from 1.5 to 2 hours, attention was given to maximizing patient comfort. The cradle uses side paddles for immobilization and incorporates an expanded foam cushion extending from the neck to the thighs, permitting patients to lie with their arms at their sides (14).

The treatment procedure used in our clinic does not include any intrafractional imaging. The only available measure of the constancy of correct target positioning throughout the treatment procedure is from an independent study of the single-fraction paraspinal treatments (19). In this study of 64 treatments, cone beam scans were taken just before and immediately after dose delivery. The mean and standard deviations of the shifts in target position during treatment in the left/right, anterior/posterior, and superior/inferior directions were small: 0.0 ± 1.4 , 0.0 ± 1.0 , and 0.0 ± 1.2 mm, respectively. Note that this is only a measure of shift in position observed at the end of treatment and therefore cannot indicate whether a target makes larger, but unknown, excursions during treatment.

Inasmuch as frequent intrafractional imaging is impractical in our clinic, patient immobilization was monitored with a stereotactic infrared tracking system developed in house. Infrared reflectors were temporarily affixed to the patient's skin in the region of the target. The reflector positions are monitored by the therapists from pretreatment imaging to the end of dose delivery. This system only serves as an alert to the therapists that a significant patient shift (>3 mm) has occurred. Should this situation persist for more than 30 seconds, the therapists stop treatment, verify target position with orthogonal radiographs, and if necessary correct the patient position. Note that the system is only useful as an alert for large shifts; it cannot be used to signal small shifts (≤ 1 mm) in target position because these are poorly correlated with changes in the patient's external contour.

The spinal cord, generally not visible in the planning CT scan, was localized using either an MRI scan or a planning scan taken with a CT myelogram. A CT myelogram involves the injection of a contrast agent into the spinal canal, rendering the cord visible in the planning CT scan. For the MRI scans, the patient was scanned while positioned in the custom immobilization cradle. The MRI-defined cord was contoured and then transferred to the coregistered planning CT scan. Both techniques have been shown to be capable of resolving the cord to within 1 mm (20). The maximum point dose to the MRI- or myelogram-defined cord was limited to either 12 or 14 Gy.

Dose-volume histograms for the GTV, PTV, and critical structures were generated by calculating the dose at 5,000 points randomly distributed within the volumes (21). In this calculation scheme, $D_{\min}$, a standard measure of dose insufficiency, is simply the lowest dose of the 5,000 points calculated. There is a limit to the accuracy with which all volumes can be defined, in part because the contours are drawn on each CT slice. The Memorial Sloan-Kettering Cancer Center treatment planning system creates a series of slabs, each centered in the CT slice and whose outline is defined by the contour. Thus, the surface of the GTV closest to the cord is not necessarily smooth but instead comprises a series of small steps. Given that the maximum dose constraint on the cord frequently results in a steep dose gradient in or near the edge of the GTV closest to the cord, it is apparent that the precise value of $D_{\min}$ will be uncertain, dependent upon the vagaries of the random point placement within each slab, and how close the corners of a slab between CT slices come to the cord. The uncertainty in $D_{\min}$ was estimated by repeating the point placement inside the volumes and recalculating the doses. With 5,000 points used, the standard deviation of $D_{\min}$ was 3.7%.

More stable measures of dose insufficiency are D_{95} and D_{98} . These are the upper limits in the range of doses in the coldest 5% of the target volume and in the coldest 2% of the target volume, respectively. Computationally, they are the doses below which there were 250 and 100 dose calculation points, respectively. The standard deviations of D_{95} and D_{98} are 0.6% and 1.0%, respectively. A tradeoff exists between numeric stability and sensitivity, however. D_{95} and D_{98} will be less sensitive to the presence of small cold spots.

The measures of dose insufficiency for the patients experiencing local failure were compared with the patient group as a whole. To determine the statistical significance of any differences between the two groups, the outcome of the study was simulated numerically, using a permutation test on the rank sum for each of the dose insufficiency measures. In the $D_{\min}$ test, for example, the treatments were ranked in order of the magnitude of $D_{\min}$. Taking no account of histology, the treatment with the lowest $D_{\min}$ was ranked as 1 and the highest as 91. Given that N failures were observed, N $D_{\min}$ ranks were randomly sampled without replacement 10^6 times, and a distribution of rank sums was generated. The rank sum of the N actual failures was used to determine the proportion of the population that randomly would have resulted in a rank sum equal to or less than the rank sum of the seven failures. Because the test being used here is two-tailed, this proportion was then doubled to obtain the p values. A similar simulation was used to investigate the influence of histology. For each histologic group, the number of random samples from that histology was made equal to the number of failures observed for that histology. As a consequence, the histologies in which no failures were observed play no part in the determination of the statistical significance in this scheme.

To investigate the influence of follow-up time, differences in Kaplan-Meier curves of freedom from local failure for patients with $D_{\min}$ equal to or less than the median $D_{\min}$, and for patients with $D_{\min}$ more than the median $D_{\min}$, were assessed using a log-rank test.

The possible confounding influence of other factors on the relationship between $D_{\min}$ and local failure was investigated by stratifying by histology, target volume, and vertebral level.

RESULTS

With a median follow-up of 18 months, seven of the 91 treated tumors (8%) had progressed at the time of this writing. The volumes associated with the failures were segmented by the neuroradiologist (E.L.). In all instances, there was overlap of the failure volume with the PTV.

The number of tumors treated, and the number that experienced local failure, are given in Table 2, grouped by histology. $D_{\min}$, D_{98} , and D_{95} are plotted in Fig. 2. Each point represents a treatment. The seven treatments that failed are indicated in magenta. Immediately apparent in the plot of $D_{\min}$ is that $D_{\min}$ was lower than average for the treatments that failed. The median $D_{\min}$ for patients experiencing local control was 15.7 Gy, whereas those experiencing local failure was 10.8 Gy. An error bar representing the 3.7% uncertainty in the determination of $D_{\min}$ has been drawn for one of the failures in the plot of $D_{\min}$. As can be seen, this uncertainty is much smaller than the range of $D_{\min}$ in the study and has little effect on the significance of the result.

Taking no account of histology, the distributions of $D_{\min}$, D_{98} , and D_{95} for the patients experiencing local failure were all found to be significantly different from the patients taken as a whole. The p values were 0.004, 0.012, and 0.031, respectively. Taking the histologic grouping specified in Table 2 into account, the results were found to be similar; $D_{\min}$, D_{98} , and D_{95} for the treatment failures were all found to be significantly different from the patient group taken as a whole, the p -values being 0.009, 0.013, and 0.045 respectively.

The log-rank test comparing Kaplan-Meier curves of freedom from local failure for patients with $D_{\min}$ less than or equal to the median $D_{\min}$ (15.1 Gy) and for patients with $D_{\min}$ greater than 15.1 Gy (Fig. 3) gave a p value <0.02 . As can be observed in Fig. 3, most failures occurred relatively early when compared with the follow-up times of either group; thus, the results are not an artifact of follow-up time.

No differences were observed in the distributions of $D_{\min}$, D_{98} , and D_{95} when grouped by histology. A Kruskal-Wallis test (10 groups) yielded p values of 0.40, 0.43, and 0.33, respectively. Test results on the subsets of patients who experienced failure ($n = 7$) and experienced control ($n = 84$) were similar. Neither was any dependence on radiosensitivity observed. Testing with three groups (I, R, S) yielded p values of 0.56, 0.45, 0.48 for $D_{\min}$, D_{98} , and D_{95} , respectively.

The possible correlation of failure with the target volume position was also investigated. In Fig. 4, the GTV volume is plotted against the location of the treated vertebra. The vertebrae locations are ordered with C1 being 1, and L5 being 24, for example. No correlations with location or target volume were observed. Neither was there any dependence of GTV volume on vertebra number; a Kruskal-Wallis test using vertebra number as a categorical variable yielded a p value of 0.24.

The delivered dose distributions will of course depend on the intrafractional target motion. Although the intrafractional target trajectory is unknown, some information was available from posttreatment imaging. Of the 7 patients experiencing local failure, posttreatment images were available for 5 of them. The shifts observed for 4 patients were less than 0.3 mm, the estimated measurement uncertainty. For 1 patient, however, the target was 1.3 mm posterior to its position at the beginning of dose delivery. Examination of the dose distribution reveals that had this shift occurred at the beginning of dose delivery and then no further target motion occurred, this would have lowered $D_{\min}$, D_{98} , and D_{95} by up to 1.5 Gy. Had this target position been used for the analysis, the significance of the results would not have changed.

DISCUSSION

The location of the disease recurrence with respect to the target is important to this analysis; clearly all seven failures were classified by the neuroradiologist and radiation oncologist as local treatment failures, not newly seeded metastases. The clinical basis for this is that the failure volume included the vertebra involved with the disease and that there was no new disease process in an adjacent vertebra. Although the follow-up MR scans are taken every 3 to 4 months, in some cases the recurrence volume had grown with sufficient rapidity to encompass most of the vertebral body and a volume of surrounding normal tissue. Thus, a direct study of the location of the initial point of failure with the delivered dose distribution is not possible. Such an investigation will be always intrinsically uncertain in this regard and will require a larger number of failures for statistical significance. Nonetheless, this investigation, while ignoring the spatial characteristics of the region of failure, has found a potentially useful correlation between a clinical definition of local failure and dosimetric measures of underdosing of the target.

The simultaneous requirements that the dose to the cord and other critical structures be kept below tolerance, and that the target be treated uniformly to the prescription dose, cannot in general be met. However, the optimization process can be controlled to some degree by the dose value of the constraints, and the relative magnitude of the penalties that are incurred when the constraints are violated. Additional constraints, not part of the optimization process for our treatment planning system, are the beam directions chosen by the planner. In

some of the dose distributions, the minimum dose to the GTV is observed to be less than the maximum cord dose. In part this has occurred because before the results of this study were known, the penalty for not meeting the minimum GTV dose was not weighted as heavily as the penalty for exceeding the cord dose, for example. However, even when the cord-dose penalty weighting is increased, the GTV $D_{\min}$ can still fall below the maximum cord dose. This occurs because of the general complexity of the plan, and the impossibility of meeting all constraints and beam-direction limitations simultaneously. Nonetheless, the weighting of the $D_{\min}$ constraint and its penalty are investigated carefully when optimizing the dose distributions.

Although the number of failures observed to date is small, the results indicate that measures of dose insufficiency in the GTV such as $D_{\min}$, D_{98} , and D_{95} may be useful in determining the risk of local failure. In particular, no failures were observed in any histology when $D_{\min}$ was >15 Gy. In 44 treatments the $D_{\min}$ was <15 Gy; thus, the percentage of local failures in this group approximately doubles to 16%.

The close proximity of part of a metastatic spinal lesion to the spinal cord presents a significant challenge to radiotherapy, even when the most technologically advanced planning and delivery systems are used. Clinical judgment must be used to balance the risk of complications against increased risk of local failure. The evidence presented here is a first step in providing the vital information required for making such decisions in a rational way.

References

1. Yamada Y, Bilsky MH, Lovelock DM, et al. High-dose, single-fraction image-guided intensity-modulated radiotherapy for metastatic spinal lesions. *Int J Radiat Oncol Biol Phys.* 2008; 71:484–490. [PubMed: 18234445]
2. Chang EL, Shiu AS, Mendel E, et al. Phase I/II study of stereotactic body radiotherapy for spinal metastasis and its pattern of failure. *J Neurosurg Spine.* 2007; 7:151–160. [PubMed: 17688054]
3. De Salles AA, Pedrosa AG, Medin P, et al. Spinal lesions treated with Novalis shaped beam intensity-modulated radiosurgery and stereotactic radiotherapy. *J Neurosurg.* 2004; 101(Suppl 3): 435–440. [PubMed: 15537201]
4. Gerszten PC, Burton SA, Ozhasoglu C, et al. Radiosurgery for spinal metastases: Clinical experience in 500 cases from a single institution. *Spine.* 2007; 32:193–199. [PubMed: 17224814]
5. Gibbs IC, Kammerdsupaphon P, Ryu MR, et al. Image-guided robotic radiosurgery for spinal metastases. *Radiother Oncol.* 2007; 82:185–190. [PubMed: 17257702]
6. Ryu S, Rock J, Rosenblum M, et al. Patterns of failure after single-dose radiosurgery for spinal metastasis. *J Neurosurg.* 2004; 101(Suppl 3):402–405. [PubMed: 15537196]
7. Ryu S, Fang Yin F, Rock J, et al. Image-guided and intensity-modulated radiosurgery for patients with spinal metastasis. *Cancer.* 2003; 97:2013–2018. [PubMed: 12673732]
8. Sahgal A, Larson DA, Chang EL. Stereotactic body radiosurgery for spinal metastases: A critical review. *Int J Radiat Oncol Biol Phys.* 2008; 71:652–665. [PubMed: 18514775]
9. Bilsky MH, Yamada Y, Yenice KM, et al. Intensity-modulated stereotactic radiotherapy of paraspinal tumors: A preliminary report. *Neurosurgery.* 2004; 54:823–830. discussion 830–821. [PubMed: 15046647]
10. Shiu AS, Chang EL, Ye JS, et al. Near simultaneous computed tomography image-guided stereotactic spinal radiotherapy: An emerging paradigm for achieving true stereotaxy. *Int J Radiat Oncol Biol Phys.* 2003; 57:605–613. [PubMed: 14529763]
11. Mahan SL, Ramsey CR, Scaperth DD, et al. Evaluation of image-guided helical tomotherapy for the retreatment of spinal metastasis. *Int J Radiat Oncol Biol Phys.* 2005; 63:1576–1583. [PubMed: 16125871]
12. Gerszten PC, Welch WC. Cyberknife radiosurgery for metastatic spine tumors. *Neurosurg Clin North Am.* 2004; 15:491–501.

13. Chang SD, Main W, Martin DP, et al. An analysis of the accuracy of the CyberKnife: A robotic frameless stereotactic radiosurgical system. *Neurosurgery*. 2003; 52:140–146. discussion 146–147. [PubMed: 12493111]
14. Lovelock DM, Hua C, Wang P, et al. Accurate setup of paraspinal patients using a noninvasive patient immobilization cradle and portal imaging. *Med Phys*. 2005; 32:2606–2614. [PubMed: 16193791]
15. Ryu SI, Chang SD, Kim DH, et al. Image-guided hypo-fractionated stereotactic radiosurgery to spinal lesions. *Neurosurgery*. 2001; 49:838–846. [PubMed: 11564244]
16. Yamada Y, Lovelock DM, Bilsky MH. A review of image-guided intensity-modulated radiotherapy for spinal tumors. *Neurosurgery*. 2007; 61:226–235. discussion 235. [PubMed: 17762734]
17. Yenice KM, Lovelock DM, Hunt MA, et al. CT image-guided intensity-modulated therapy for paraspinal tumors using stereotactic immobilization. *Int J Radiat Oncol Biol Phys*. 2003; 55:583–593. [PubMed: 12573745]
18. Kriminski SA, Lovelock DM, Seshan VE, et al. Comparison of kilovoltage cone-beam computed tomography with megavolt-age projection pairs for paraspinal radiosurgery patient alignment and position verification. *Int J Radiat Oncol Biol Phys*. 2008; 71:1572–1580. [PubMed: 18539405]
19. Lovelock DM, Wang P, Amols HI, et al. Intra-fractional motion of bony targets in the spine and pelvis during extra-cranial SRS treatment. *Med Phys*. 2008; 35:2831.
20. Thariat J, Castelli J, Chanalet S, et al. CyberKnife stereotactic radiotherapy for spinal tumors: Value of computed tomographic myelography in spinal cord delineation. *Neurosurgery*. 2009; 64:A60–A66. [PubMed: 19165075]
21. Niemierko A, Goitein M. Dose-volume distributions: A new approach to dose-volume histograms in three-dimensional treatment planning. *Med Phys*. 1994; 21:3–11. [PubMed: 8164585]

Fig. 1.

Lesion at L1. The gross target volume is shown in light blue. The clinical target volume (orange) encompasses the vertebral body. The planning target volume is constructed using a 0.3-cm margin on the clinical target volume, except in the vicinity of the cauda (yellow). Another critical structure, the left kidney, is shown in green. The prescription isodose (magenta) does not fully enclose the planning target volume or the clinical target volume.

Fig. 2.

(a) D_{min} , (b) D_{98} , and (c) D_{95} grouped by histology. Each point is a treatment. Local failures are indicated in magenta. The error bars are representative and indicate the uncertainty in the computation of D_{min} , D_{98} , and D_{95} .

Fig. 3. Kaplan-Meier curves of freedom from local failure for (1) Patients with $D_{\min} \leq$ the median $D_{\min}$ (15.1 Gy), and (2) Patients with $D_{\min} > 15.1$ Gy. The median followup was 17.5 months for patients with $D_{\min} < 15.1$ Gy, and 19 months for patients with $D_{\min} > 15.1$ Gy.

Fig. 4. Gross target volume (GTV) as a function of vertebral location. Each point is the GTV of an individual treatment. Local failures are indicated in magenta.

Table 1

Summary of important normal tissue constraints used in single-fraction treatment of bony metastases

Structure	Limit
Spinal cord	14 Gy maximum point dose to myelogram or MRI-defined cord.
Cauda equina	16 Gy maximum point dose to myelogram or MRI-defined cauda.
Esophagus	15 Gy to 2 cc or less
Liver	15% normal tissue complication probability using the Lyman mean dose model ($n = 1$, $m = 0.12$, $\alpha/\beta = 3$)
Stomach/ bowel	15–16 Gy maximum point dose (to volume), 12 Gy maximum circumferential dose on any single slice
Kidney	10 Gy maximum mean dose; spare the other kidney

Table 2

Histologies and failure times

Histology	Radiosensitivity (R: resistant S: sensitive I: indeterminate)	number of lesions treated	No. of treatments resulting in local failure	Time to local failure (mo)
Sarcoma	I	10	0	—
Renal cell	R	18	1	19
Prostate	S	11	2	5, 9
Melanoma	R	12	1	13
Lung	R	5	0	—
Head and neck	R	9	1	5
Gastrointestinal	R	20	1	2
Breast	S	4	0	—
Bladder	S	1	0	—
Leydig cell	I	1	1	1
Total		91	7	(median: 5)