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Use of Spinal Cord Diffusion Tensor Imaging to Quantify Neural Ablation and Evaluate Outcome after Percutaneous Cordotomy for Intractable Cancer Pain

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Abstract

Background—Up to 20% of patients experience only partial pain relief after percutaneous cordotomy for cancer pain.

Objective—To determine whether diffusion tensor imaging (DTI) can quantify neural ablation and help evaluate early postoperative outcomes after cordotomy.

Methods—Patients undergoing percutaneous CT-guided cordotomy for intractable cancer pain were prospectively studied. Pre- and postoperative assessment was made using the visual analog scale (VAS) on pain and the pain severity scores of the Brief Pain Inventory Short Form. On postoperative day 1, DTI images of the high cervical spinal cord were obtained. DTI metrics were correlated with the number of ablations as well as early postoperative pain outcomes.

Results—Seven patients (4 male, mean age 53.8 ± 4.6 years) were studied. Fractional anisotropy of the hemicord was significantly lower on the side of the lesion as compared to the contralateral side (0.54 ± 0.03 vs. 0.63 ± 0.03 , $p < 0.001$). Mean diffusivity correlated with the improvement in the VAS score at 1 week ($r = 0.88$, 95% CI = 0.34–1.00, $p = 0.008$), as well as the change in pain severity scores at 1 week ($r = 0.99$, 95% CI = 0.82–1.00, $p < 0.001$).

Conclusion—DTI metrics are sensitive to the number of ablations as well as early improvement in pain scores after cordotomy. DTI of the cervical spinal cord is a potential biomarker of neural ablation after percutaneous cordotomy for intractable cancer pain.

Keywords

Percutaneous cordotomy; Cancer pain; Diffusion tensor imaging; Ablation; Fractional anisotropy; Mean diffusivity

Introduction

Percutaneous cordotomy for cancer-related pain is successful in more than 80% of patients [1–3]. However, a proportion of patients experience no relief or only transient or partial relief after the procedure. One of the potential causes is an incomplete ablation of the spinothalamic tract. Using radiofrequency technology, surgeons can control the temperature and duration of radiofrequency lesions [4, 5]; however, the actual extent of neural ablation is not known. It is possible that identical parameters during lesioning may produce different degrees of neural ablation among different patients.

Diffusion tensor imaging (DTI) measures the magnitude of water molecular diffusion within tissues and detects the preferential diffusion in a particular direction [6]. DTI is able to characterize microstructural changes within neural tissues, such as the spinal cord, and has been used to assess spinal cord lesions after spinal cord injury [7, 8] as well as microstructural changes in patients with cervical spondylotic myelopathy [9, 10]. To date, the role of DTI in characterizing the lesion produced by cordotomy has not been explored.

The present study aimed to determine whether microstructural changes of the cordotomy lesion assessed by spinal cord DTI could improve the evaluation of postoperative outcomes after percutaneous cordotomy for intractable cancer pain.

Methods

This study was undertaken at the University of Texas M.D. Anderson Cancer Center, Houston, TX, USA. The patients in this report are part of a prospective clinical trial being conducted at our institution, the results of which will be published separately. Patients with medically refractory unilateral cancer-related pain below the C5 dermatome, and with a pain intensity 4 out of 10 (in whom the pain goal was exceeded) were included in this study. All patients underwent percutaneous CT-guided cordotomy for intractable cancer pain and postoperative MRI. This study was approved by our Institutional Review Board.

Clinical Evaluation

After informed consent had been obtained, the preoperative evaluation of pain was assessed with the visual analog scale (VAS) score – scored from 0 (no pain) to 10 (worst pain) – and the Brief Pain Inventory Short Form (BPI-SF) on the day before the cordotomy. Postoperative pain was assessed using the VAS and BPI-SF on day 7 after the cordotomy. The VAS score represents the average pain experienced by the patient over the previous 24 h. The BPI-SF is a valid and reliable instrument and has been used widely to measure cancer

pain [11, 12]. For the present study, the *pain severity score* of the BPI-SF (average score for questions 3–6) [13] was used for analysis.

Surgical Technique

All cordotomies were performed using a radiofrequency ablation technique (G4 radiofrequency generator and LCED disposable cordotomy electrode, Cosman Medical, Burlington, MA, USA). In most cases, a myelogram was performed prior to the procedure in a fluoroscopy suite. Procedures were performed at the C1–C2 level using intraoperative CT scan guidance. Intravenous sedation with opioids, and either propofol or dexmedetomidine, was used for patient comfort.

Multiple, limited, short-segment axial CT scans (Fig. 1) were performed to facilitate the advancement of the spinal needle to the anterolateral quadrant of the spinal cord. When the radiofrequency electrode was abutting the anterolateral cord, the radiofrequency electrode with an exposed tip of 2 mm and a diameter of 0.2 mm was introduced into the spinal cord parenchyma. Once the patient was fully awake and conversant, intraoperative testing was performed. A safe distance from the corticospinal tract was verified by ensuring that motor stimulation (2 Hz, 100 μ s pulse width) did not elicit contractions below 1 V. Presence within the spinothalamic tract was confirmed by sensory stimulation (100 Hz, 100 μ s) which elicited contralateral paresthesias, optimally in the area of pain, at a voltage less than 0.2 V.

We have found that 2–3 radiofrequency ablations at 80 °C led to adequate lesioning of the spinothalamic tract. Between ablations, clinical testing using a safety pin was performed to assess for the development of hypesthesia, particularly in the region of pain. In addition, repeat sensory stimulation was performed between ablations to assess whether the threshold for eliciting paresthesias from the spinothalamic tract had elevated from the preablation threshold. A third ablation was performed if hypesthesia was not present shown by the clinical examination, or if there was no elevation in the threshold for sensory stimulation.

Imaging

High-resolution MRI of the cervical spine was obtained on postoperative day 1. Sagittal and axial T2-weighted images were obtained of the cervical spine. The DTI protocol included a TR/TE of 4,000/70 ms, field of view of 18–22 cm, phase 0.5, 3 mm slice thickness, and voxel size of $1.5 \times 1.5 \times 3.0$ mm. A *b*-value of 500–600 s/mm² was used with 12–16 diffusion directions. The scan time for the DTI scan was 7–10 min. Data were acquired on GE wide-bore 3- and 1.5-T systems.

The MedINRIA software package (www.sop.inria.fr/asclepios/software/MedINRIA) was used to analyze the DTI scans. Axial fractional anisotropy (FA) maps through the lesion were selected, and FA was calculated voxel by voxel using manually drawn regions of interest. Regions of interest were drawn for the hemicord on the side of the lesion as well as on the contralateral side (Fig. 2). The regions of interest were drawn within the perimeter of the cord so as to avoid partial volume effects due to cerebrospinal fluid. Mean FA and mean diffusivity (MD) of all selected axial slices were used for analysis.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 (Chicago, IL, USA). The paired *t* test was used to compare the DTI metrics of the lesioned hemicord and the contralateral side. Correlations between DTI metrics, VAS scores and the pain severity scores of the BPI-SF were performed using Spearman's correlation. Means were reported as $\pm$ standard deviation, and the level of significance was set at $p < 0.05$.

Results

Seven consecutive patients (4 male, 3 female, mean age 53.8 ± 4.6 years) were studied. Preoperative demographic and clinical data are described in Table 1. Three patients underwent 3 radiofrequency ablations, and 3 patients underwent 2 radiofrequency ablations. One patient underwent 4 radiofrequency ablations. One patient (patient 2) experienced intraoperative motor stimulation prior to ablation, and this was associated with dorsomedial penetrations of the spinal cord. In 1 patient (patient 5), sensory stimulation in the area of pain was elicited at a higher threshold than expected (0.3 V), and despite 3 ablations in the anterolateral spinal cord, the patient did not have satisfactory outcomes.

Clinical Evaluations

The median preoperative VAS score was 7 (range 4–9), and the median postoperative score was 1 (range 0–5). The median preoperative pain severity score was 5.25 (range 3.75–6.25), and the median postoperative pain severity score was 1.5 (range 0–4.75). Pain severity scores were not available for 1 patient.

DTI Metrics

FA of the hemicord on the side of the lesion was significantly lower as compared to the contralateral side (0.54 ± 0.03 vs. 0.63 ± 0.03 , $p < 0.001$). FA of the lesion was significantly lower in patients with more than 2 ablations ($n = 4$) as compared to those with 2 ablations ($n = 3$; 0.52 ± 0.02 vs. 0.56 ± 0.01 , $p = 0.04$). FA was also significantly correlated with the number of ablations ($r = -0.81$, 95% CI from -0.19 to -0.99 , $p = 0.03$). Although the MD on the side of the lesion was higher than the contralateral side, this did not reach statistical significance (2.6 ± 0.68 vs. 2.45 ± 0.67 , $p = 0.35$).

Clinical Correlates of DTI Metrics

MD of the hemicord on the side of the lesion also correlated with the change in VAS score at 1 week ($r = 0.88$, 95% CI = 0.34 – 1.00 , $p = 0.008$). MD correlated with the change in pain severity scores at 1 week ($r = 0.99$, 95% CI = 0.82 – 1.00 , $p < 0.001$) (Fig. 3). FA did not correlate with the change in VAS score at 1 week ($r = -0.43$, 95% CI from -1.00 to 1.00 , $p = 0.33$) or the change in pain severity scores at 1 week ($r = -0.06$, 95% CI from -1.00 to 1.00 , $p = 0.91$).

Discussion

The present study shows that DTI of the high cervical cord can detect microstructural changes created by the cordotomy lesion. Our results also indicate that increased DTI

metrics of the lesion correlates with improvement in the VAS and the pain severity scores as measured using the BPI-SF at 1 week after the procedure. These preliminary results point to the potential use of DTI to quantify neural ablation after cordotomy and evaluate patients who have a suboptimal surgical outcome.

DTI metrics provide a measure of microstructural changes within neural tissues [14]. FA, which measures the degree of anisotropy, is decreased in the presence of axonal injury due to interruption of longitudinally aligned axons. In the present study, the cordotomy lesion produced a decrease in FA. The decrease in FA within the cordotomy lesion is consistent with the changes in DTI metrics observed after acute neural injury in other models. Animal studies of experimental spinal cord injury have shown an early decrease in FA after the injury [15]. Human studies in acute spinal cord injury have also described a significant decrease in FA in early spinal cord DTI after the injury [8, 16]. In the present study, changes in FA were sensitive to the number of ablations performed during the procedure. These results indicate that DTI can noninvasively detect and measure changes in spinal cord microstructure created by cordotomy.

There are limited data on the evaluation of patients who have poor pain relief or early recurrence of pain after cordotomy. While patient selection is one of the most important factors contributing to outcome, optimizing surgical technique and creating a discrete effective lesion is essential. Mooij et al. [17] reported that inadequate lesioning and the presence of alternate pain pathways was the likely etiology for patients with no pain relief or early recurrence of pain after the procedure. Our study shows that there is significant variability in the microstructural changes of the lesion as measured by DTI, and this may be due to differences in tissue properties of the cord between patients. Prior animal studies have acknowledged considerable variability in the size of a radiofrequency lesion due to position of the electrode in relation to the CSF-tissue interface [18], as well as differences in tissue resistance and microcirculation [19, 20]. MD, which measures the average of 3 tensors in the principal axes [6], can be increased due to the disruption of membranes, cellular edema, or demyelination produced by radiofrequency ablation of neural tissues [21]. In the present study, a high MD of the cordotomy lesion correlated with greater improvement in VAS pain scores and the pain severity scores. A lower MD of the cordotomy lesion, therefore, possibly indicates inadequate neural ablation. DTI metrics of the lesion can therefore assist surgeons in understanding whether inadequate neural ablation is the cause of poor pain outcomes. Further management of these patients may include an open thoracic cordotomy, which has been performed as a second-line treatment option in select patients with refractory lower quadrant or extremity pain [22, 23].

This study represents one of the first to use advanced MRI to analyze the spinal cord lesion produced by cordotomy. We present our preliminary experience with this technique and show the feasibility of performing early postoperative spinal cord DTI after cordotomy and its utility in quantifying neural ablation. DTI scans can be performed on 1.5- or 3-T MR machines with scan times of less than 20 min. Limiting the duration of scanning is an important factor, since patients with intractable cancer pain may find it difficult to lie still for prolonged periods of time, and image quality can suffer significantly from motion. Early postoperative imaging allows us to determine the predictive value of DTI metrics for pain

outcomes at the follow-up as well as offers a practical time point since many of these patients are hospitalized for at least 24 h after the procedure. However, hemorrhage and edema within the lesion may affect DTI metrics and assessment of neural ablation soon after the procedure. DTI metrics after neural injury can change over time, and the results of the present study apply to early postoperative imaging after cordotomy.

This study is limited by the small number of patients studied and the lack of long-term outcomes. In this patient population, however, early efficacy of the procedure is important given potentially short survival times from malignancy. Future studies could use high-resolution scans and tract-specific DTI metrics to analyze which anatomical pathways have been lesioned during the procedure. Such investigations could also enhance our understanding of the pain pathways that need to be targeted to improve outcomes after cordotomy for intractable cancer pain.

Conclusions

DTI of the spinal cord detects microstructural changes within the lesion after cordotomy, and MD of the lesion correlates with early postoperative outcomes after cordotomy. DTI of the cervical spinal cord is a potential biomarker of neural ablation after percutaneous cordotomy for intractable cancer pain.

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Fig. 1.
a Axial CT image of the cervical spinal cord during the cordotomy procedure showing the electrode entering the right anterolateral quadrant of the spinal cord. **b** Postoperative axial T2-weighted image of the cervical spinal cord at the C1–C2 level showing a hyperintense lesion (arrow) in the right anterolateral quadrant of the spinal cord.

Fig. 2. T2-weighted and DTI MRI images following percutaneous CT-guided cordotomy at the C1–C2 level. **a** Sagittal T2-weighted image of the cervical spine showing T2-weighted hyperintensity at the C1–C2 level within the ventral half of the cervical cord. **b** Axial T2-weighted image at the level of the lesion showing hyperintensity in the left anterolateral quadrant, which was targeted for cordotomy. **c** A representation of the manual regions of interest for each hemicord superimposed on the axial T2-weighted image.

Fig. 3. Scatter plot showing correlation between MD of the hemicord on the side of the lesion and change in VAS score at 1 week (a) and change in pain severity score as measured by the BPI (b).

Demographic and clinical features of patients with intractable cancer pain undergoing percutaneous CT-guided cordotomy

Table 1

Subject No.	Age, years	Sex	Malignancy	Location of pain	Lesions, <i>n</i>
1	43	Male	Rectal cancer	Buttock	2
2	66	Female	Unknown primary	Hip	3
3	54	Female	Lung cancer	Chest	2
4	52	Female	Gastric cancer	Groin/thigh	3
5	67	Male	Lung cancer	Chest	3
6	61	Male	Prostate cancer	Groin/leg	2
7	34	Male	Melanoma	Right leg	4