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Potential Usefulness of ^{18}F-2-Fluoro-Deoxy-D-Glucose Positron Emission Tomography in Cervical Compressive Myelopathy

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Study Design. This case study describes the usefulness of high-resolution ^{18}F-2-fluoro-deoxy-D-glucose (^{18}FDG)–positron emission tomography (PET) for metabolic neuroimaging of the cervical spinal cord in patients with compressive myelopathy.

Objective. To examine whether ^{18}FDG-PET imaging could visualize deterioration of cervical spinal cord function associated with a variable degree of compression and to determine its potential usefulness during assessment of myelopathy.

Summary of Background Data. A few studies have described the use of ^{18}FDG-PET imaging in cervical cord diseases, but visualization of the cervical spinal cord before and after surgical decompression for compressive myelopathy has not been reported. The potential usefulness of ^{18}FDG-PET imaging for assessment of the function of compressed cervical cord has not been discussed previously.

Methods. An ^{18}FDG-PET scan was performed before and after surgery in seven patients with cervical compressive myelopathy. The correlation between the metabolic rate of glucose of the cervical spinal cord and neurologic scores was evaluated. The metabolic rate of glucose in different vertebral levels was also measured.

Results. Preoperative metabolic rate of glucose was high in two patients but low in the other five. At the time of the second postoperative examination, metabolic rate of glucose was higher in six of the seven patients, and the increase was associated with neurologic improvement. Use of ^{18}FDG was not related to changes in signal intensities on T2-weighted magnetic resonance images. The metabolic rate of glucose decreased at the affected vertebral level in four patients, increased in two, and did not change in one, relative to the unaffected levels.

Conclusions. High-resolution ^{18}FDG-PET neuroimaging may provide clinically useful qualitative and quantitative estimation of impaired metabolic activity of the compromised cervical spinal cord in compressive myelopathy. ^{18}FDG-PET images may also offer additional information related to neuronal dysfunction induced by mechanical compression. [Key words: cervical myelopathy, ^{18}F-2-fluoro-deoxy-D-glucose, metabolic rate of glucose, positron emission tomography, spinal cord] **Spine 1999;24:1449–1454**

Assessment of the neurologic function of the compromised cervical spinal cord is important during surgical treatment of the condition, but most conventional tests are designed to assess deterioration of neural conductivity[2] and/or morphologic changes[3,5] of the compressed cord. Another form of diagnostic procedure, metabolic neuroimaging by positron emission tomography (PET),[6–9] has been used to investigate the metabolic activity of neural tissues.[10,20,24] Visualization and quantification of metabolic activity of the cervical cord by PET may be of value during the course of treatment of cervical compressive myelopathy. In a pilot study using ^{18}F-2-fluoro-deoxy-D-glucose (^{18}FDG)-PET in a group of patients with cervical myelopathy, we demonstrated that the ^{18}FDG utilization rate in the cervical cord correlated with the neurologic score.[6,16] Based on these results, we postulated that ^{18}FDG-PET may be used for assessing certain aspects of cervical cord function that cannot be assessed otherwise by conventional tests such as magnetic resonance imaging (MRI).

The current case study was therefore designed to quantify the metabolic utilization rate of ^{18}FDG in patients with cervical compressive myelopathy before and after surgery. The potential usefulness of metabolic neuroimaging by ^{18}FDG-PET is also discussed.

■ Patients and Methods

Patients and Assessment. The study involved seven patients with cervical compressive myelopathy who volunteered for preoperative and postoperative ^{18}FDG-PET evaluation. Their neurologic symptoms were assessed according to the Japanese Orthopaedic Association scoring system (Table 1).[14] Their ages at operation ranged from 42 to 68 years. Postoperative PET examination was performed 2.0 to 2.5 years after surgery (average, 2.2 years).

Routine radiologic examination included MRI (1.5 Tesla Signa, General Electric, Milwaukee, WI). On T2-weighted MR images, changes in signal intensity within the cervical cord around the level(s) of compression were carefully recorded, and the findings were classified as hyperintense, isointense, and hypointense signals, as described previously by our group.[2]

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Table 1. The Japanese Orthopaedic Association Scoring System for Assessment of Cervical Myelopathy[14]

Category	Score (points)
I. Motor function of the upper extremity	
Unable to eat with either chopsticks or a spoon	0
Able to eat with a spoon, but not with chopsticks	1
Able to eat with chopsticks, but inadequately	2
Able to eat with chopsticks, but awkwardly	3
Normal	4
II. Motor function of the lower extremity	
Unable to walk	0
Needs a cane or other walking aid on flat ground	1
Needs walking aid only on stairs	2
Able to walk unaided, but slowly	3
Normal	4
III. Sensory function	
(a) Upper extremity	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
(b) Lower extremity	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
(c) Trunk	
Apparent sensory disturbance	0
Minimal sensory disturbance	1
Normal	2
IV. Bladder function	
Urinary retention or incontinence	0
Severe dysuria (sense of retention)	1
Slight dysuria (pollakiuria, retardation)	2
Normal	3

Note: The score in a normal subject is the total of the best scores: (I + II + III + IV) = 17 points.
The extent (rate) of neurological improvement is obtained as follows:

$$Extent\ (\%) = \frac{Postoperative\ score - Preoperative\ score}{17 - preoperative\ score} \times 100$$

The ^{18}FDG-PET protocol together with MR imaging strictly followed the Ethical Committee Guidelines of Fukui Medical University, and written informed consent was obtained from each patient.

Positron Emission Tomography. The GE Advance System (GE-YMS, Tokyo, Japan) was used for the tracer technique. The physical characteristics of the scanner have been described by De Grado et al.[7] The system allows simultaneous acquisition of 35 transverse slices with interslice spacing of 4.25 mm and also offers a two-dimensional view of the images. The field of view and pixel size of the reconstructed images were 256 mm and 2 mm, respectively. The subjects were examined after they fasted for more than 4 hours. Transmission scans were obtained over 10 minutes using a standard pin source of ^{68}Ge/^{68}Ga for attenuation correction of the emission images. A dose of 244 to 488 MBq (average, 357 MBq or 9.6 mCi) of ^{18}FDG was injected into the cephalic or basilic vein over a period of 10 seconds. Dynamic scans were also obtained from the subjects up to 60 minutes after injection of ^{18}FDG. Intermittent manual blood sampling from the radial or ulnar artery was also performed on the side opposite that of tracer injection. After injection of ^{18}FDG, 2-mL blood samples were obtained every 15 seconds in the first 2 minutes, and then at 2.5, 3, 5, 10, 15, 20, 30, 45, and 60 minutes after injection. Using a cylindrical phantom filled with the ^{18}FDG solution, plasma radioactivity was measured by the scintillation counter against which the PET camera was cross-calibrated.

The images obtained by the PET camera were processed on a computer workstation (Sparc 20; Sun Microsystems, Mountain View, CA), using commercial software (DoctorView; Asahikasei, Nobeoka, Japan). To provide a quantitative analysis, the metabolic rate of glucose (MRglc) was calculated using Sokoloff's three-compartment model[21] and an autoradiographic technique with *a priori* estimates of the rate constants and lumped constant of normal cerebral gray matter.[13] A round (10.3 mm in diameter, 21 pixels) region of interest (ROI) was selected that was slightly larger than the anteroposterior diameter of the cervical cord of normal adult Japanese subjects.[3,5,19] The ROI was placed on the cord in every transaxial slice, and sagittal images were used as an "on-line" reference to place the ROI. During placement of the ROI, a sagittal MR image served as a reference to match the level of the ROI on the spinal cord. The maximum count in the ROI was then used as the tissue radioactivity to minimize the ROI effect.[12,17] The ROIs in each vertebral segment (C2–C3, C3–C4, C4–C5, and C5–C6) were averaged to represent MRglc at each level. In addition, ROIs were averaged across all cervical segments, representing the metabolic activity of the cervical spinal cord.

■ Results

Clinical Presentation and Magnetic Resonance Imaging

Table 2 shows the anthropometric data, the level of the affected vertebrae, and neurologic scores. Neurologic improvement was noted after decompression in all pa-

Table 2. Clinical Data

Case No.	Age (yr) (gender)	Disease	Affected Levels	Surgical Procedures	JOA Scores[14] (before → after surgery)	Extent of Improvement (%)	Follow-up (yr)
1	49 (F)	CDH	C5–C6	Ant	14 → 16	66.7	2.5
2	52 (F)	CSM	C5–C6	Ant	12 → 16	80.0	2.4
3	42 (F)	OPLL	C5–C6, C6–C7	Subt and Post	15 → 16	50.0	2.3
4	53 (M)	CDH	C3–C4	Ant	9 → 12	37.5	2.1
5	66 (M)	CDH	C3–C4	Ant	10 → 16	85.7	2.1
6	68 (M)	CSM	C4–C5	Post	11 → 13	33.3	2.0
7	57 (M)	CSM	C6–C7	Ant	15 → 16	50.0	2.0

CDH = cervical disc herniation; CSM = cervical spondylotic myelopathy; OPLL = ossification of the posterior longitudinal ligament; Ant = anterior decompression (Robinson's procedure); Post = C3–C7 laminoplasty; Subt = subtotal spondylectomy.

Table 3. Results of Positron Emission Tomography

Case No.	Average Metabolic Rate of Glucose (mg/min per 100 g brain)	
	Preoperative	Follow-up
1	1.85	1.87
2	1.65	1.78
3	2.62	2.63
4	1.77	2.25
5	1.96	2.20
6	1.90	1.98
7	2.46	2.34

tients, although the extent of improvement varied from one subject to another, ranging from 33.3% to 85.7%.

An MRI showed hyperintense signals on T2-weighted images in six patients (cases 1 through 6) at the affected vertebral level(s) before surgery, whereas one patient with a slight paresis (case 7) showed isointense signal at the affected level. After surgery, none showed significant changes in signal intensities on T2-weighted images at the surgical segments.

Positron Emission Tomography

Data of preoperative and postoperative ^{18}FDG-PETs are summarized in Table 3. The preoperative MRglc value averaged across the entire cervical spinal cord was higher than normal[16] in two patients (cases 3 and 7), whereas others showed low values. After surgery, the average MRglc increased in all but one patient (case 7) who showed a very small reduction. Two patients (cases 4 and 5; Figure 1, A through E) showed a large increase in average MRglc after surgery, but the extent of neurologic improvement differed widely among patients.

The estimated MRglc at the affected vertebral level did not show a consistent pattern relative to that of unaffected segments. For example, it was lower in four patients (cases 1, 2, 4, and 5), higher in two (cases 3 and 7), and not different in one (case 6; Figure 2, A through E) relative to the unaffected segments.

■ Discussion

In several studies, investigators have assessed cervical spinal cord function in a variety of pathologic condi-

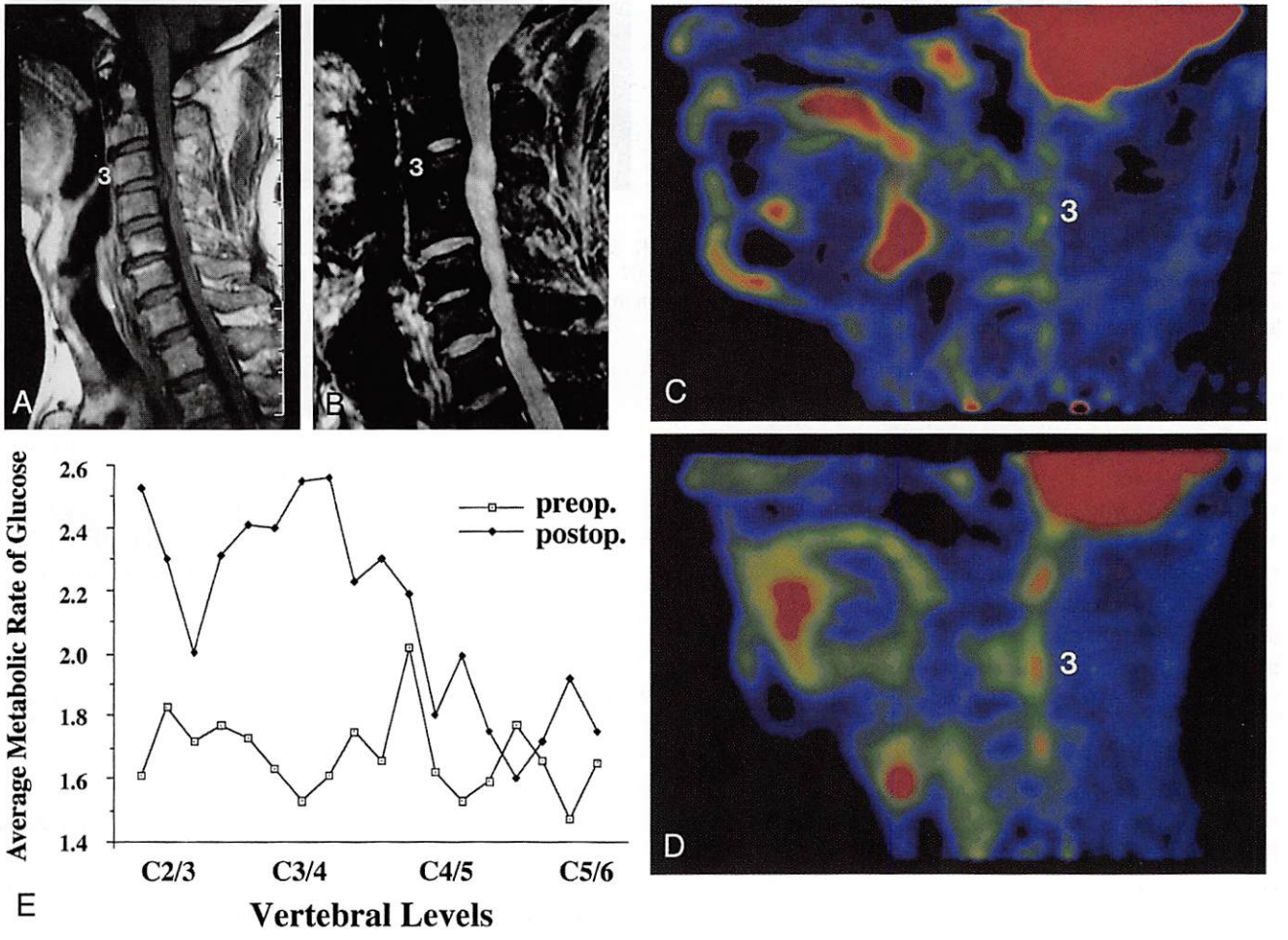

Figure 1. Preoperative (**A**) T1-weighted (TR, 400 msec; TE, 50 msec) and postoperative (**B**) T2-weighted (TR, 1000 msec; TE, 100 msec) spin–echo magnetic resonance images of a representative patient (case 5) showing a large herniated disc at C3–C4 and excellent decompression, respectively. Positron emission tomography image of case 5 before (**C**) and after (**D**) anterior decompression. 3 = location of C3. Surgery produced a significant increase in the average metabolic rate of glucose (shown in milligrams per minute per 100 g brain) at the level of decompression (**E**).

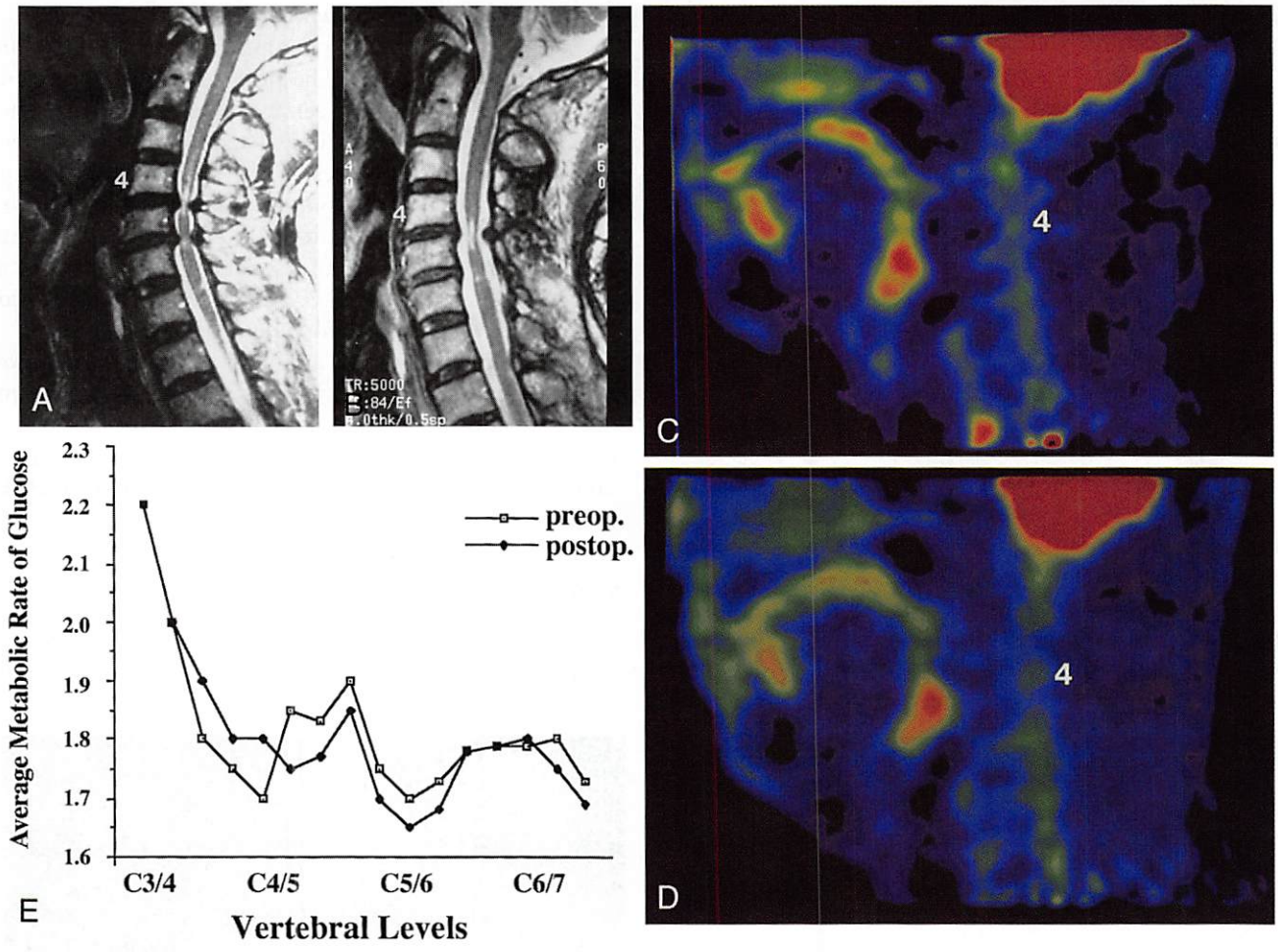

Figure 2. Preoperative (**A**) and postoperative (**B**) T2-weighted (TR, 5000 msec; TE, 84 msec) magnetic resonance images of case 6. Positron emission tomography images before (**C**) and after (**D**) C3–C7 laminoplasty[3,5] are also shown. 4 = location of C4. There are no significant changes in the average metabolic rate of glucose (shown in milligrams per minute per 100 g brain) between different vertebral levels and between preoperative and postoperative images (**E**).

tions.[2,3,5,23] Because profound paresis is a physical sign reflecting serious spinal cord damage, in the current study, neurologic symptoms were examined, as well as surgical outcome, in relation to abnormal findings on MRIs and spinal cord–evoked potentials.[2,3,5] In addition, similar to its clinical application to neural tissues other than the spinal cord,[10,13,24] PET imaging may be useful for demonstrating the biologic activity of the compromised cervical cord if the tracer technique and image processing are correctly applied.

Di Chiro et al[8,9] were the first investigators to visualize and quantitate the ^{18}FDG utilization rate in the cervical cord in 34 patients with tumors and in healthy volunteers, using a high-resolution PET scanner (Neuro-PET, National Institutes of Health, Bethesda, MD) with a maximum resolution of 6 mm. They found that the average normal MRglc of the upper cervical cord was 1.7 ± 0.6 mg/100 g · min. Using the ^{11}C-methionine-PET technique, Higano et al[11] observed the pathologic viability of a cervical intramedullary ependymoma. The current study also involved patients with profound myelopathy who had a low MRglc compared with healthy subjects and demonstrated that the MRglc measured before surgery correlated with the postoperative neurologic score.[6] The findings may reflect reduced metabolic activity in the cervical cord or, possibly, in the motoneurons. Based on these findings, we postulated that ^{18}FDG-PET might have use to evaluate metabolic dysfunction of the cervical spinal cord that might correlate with the clinical features of myelopathy.

Glucose metabolism of the normal spinal cord was investigated by Kamoto et al[16] with ^{18}FDG using a camera similar to that used in the current study. Based on data from 23 subjects without arterial sampling, they established the presence of a significant correlation between ^{18}FDG utilization normalized to the injected dose, body weight (standardized uptake value), and age. The calculated normal MRglc of the cervical spinal cord in that study was 1.93 ± 0.37 mg/min per 100 g brain, a value similar to that reported by Di Chiro et al[8] (1.7 ± 0.6 mg/min per 100 g brain), despite differences in the spatial resolution of the PET cameras used in both studies. Because the age of the study patients (42–68 years) was similar to that of patients in the study by Kamoto et

al[16] (mean, 65.5 ± 8.5 years), the normal MRglc value of the cervical spinal cord that they reported was used to compare the results of the current study.

These results showed high MRglc values in two patients (cases 3 and 7), relative to normal values,[16] whereas other patients had low values. These findings are compatible with our preliminary findings,[6] which showed a considerable variability in glucose utilization in the cord among patients with myelopathies. Although the mechanism of such variability is unclear at present, our experimental studies[1,4,18,22] allow formulation of a possible hypothesis. We have recently demonstrated in the twy/twy mouse that compression of the spinal cord that produces 50% to 70% reduction in the transverse area of the cord is associated with increased immunoreactivity of neuropeptides (brain-derived neurotropic factor and neurotrophin-3) in neurons and some glial (astroglial) cells.[18,22] In the same experimental model, we showed a significant increase in the neuronal soma size and number of neurons, as well as the presence of a significantly elongated dendritic arbor.[22] A similar neuronal change may also occur in the cervical spinal cord of patients with myelopathies, thus explaining the increased MRglc. However, a significant compression (transverse area of the spinal cord < 50% of normal value) diminishes the number of anterior and posterior gray horn cells at the level of compression.[1,4] The condition is also found to be associated with reduced immunoreactivity of neuropeptides necessary for neuronal survival.[22] We therefore speculate that such neuronal loss and reduced immunoreactivity may result in reduced ^{18}FDG use. Thus, differences in the pathologic condition and extent of mechanical and biologic damage of the spinal cord may, singly or together, influence the glucose utilization rate. Admittedly, the current study is based on only a small sample, and a definitive conclusion must therefore be avoided. However, an extended scale of the study cohort and frequent as well as serial PET examinations will further clarify the correlation between ^{18}FDG utilization and cervical spinal cord neurology, the significance of ^{18}FDG-PET in clinical use, and the "critical point" of neurologic reversibility in cervical compressive myelopathy.

A number of technical aspects must be considered when using ^{18}FDG-PET in cervical myelopathies. The transverse area of the cervical cord is small, and thus the effect of object size on quantification during PET imaging must be carefully taken into account.[8,9,12] Di Chiro et al[8,9] have acknowledged that the major difficulty in accurate measurement of glucose utilization in this small structure of the cervical cord is the poor resolution of the positron tomographs. They recommend the use of a high-resolution scanner to compensate for the reduced area. Simultaneous acquisition of 35 different transverse slices with 4.25-mm interslice space (two-dimensional mode) is viewed by the high-resolution PET camera, as presently used. The effect of small object size may therefore be minimized by using this camera. Placement of an ROI in the multiple transverse slices of PET images may be another significant concern. Kameyama et al[15] measured the transverse area of the cervical spinal cord in cadavers of adult Japanese subjects. The mean area was 51.2 ± 5.3 mm^2 at C8 and 58.5 ± 7.2 mm^2 at C6, whereas that of the gray matter ranged from 7.2 ± 1.2 mm^2 at C3 to 10.7 ± 1.3 mm^2 at C7. In cervical compressive myelopathy, the transverse area of the spinal cord is reduced by approximately two thirds relative to the control.[3,5] When these findings are considered together, the clinician must be careful during placement of an ROI in ^{18}FDG-PET scanning in cervical compressive myelopathy.

In conclusion, neuroimaging by ^{18}FDG-PET provides qualitative and quantitative measurement of reduced metabolic activity of the compromised cervical cord in patients with compressive myelopathy. The current results indicate that PET imaging is potentially useful for the assessment of metabolic activity of the compromised cervical cord, which is impossible by other conventional neurodiagnostic methods.

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