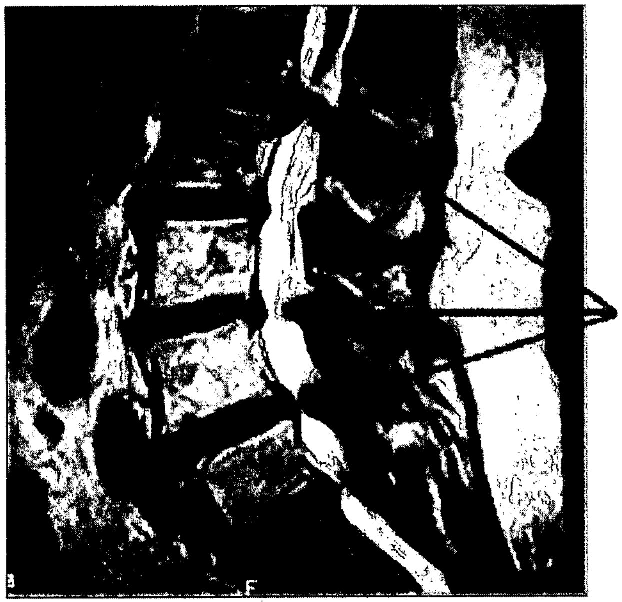
誘発磁界測定を用いた腰部脊柱管狭窄症の電気生理学的評価

Lumber Canal Stenosis



multiple stenosis

but

symptomatic?

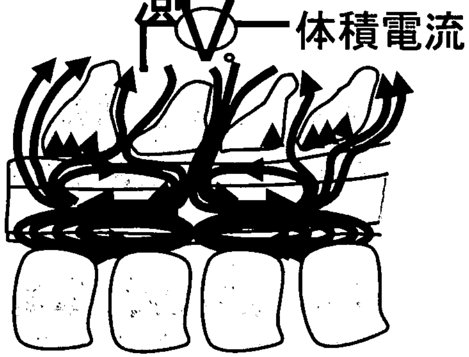
高齢者の腰部脊柱管狭窄症では複数の高位において狭窄を認めることも多く、多椎間の手術が患者に身体的負担を負わせることは少なくない。

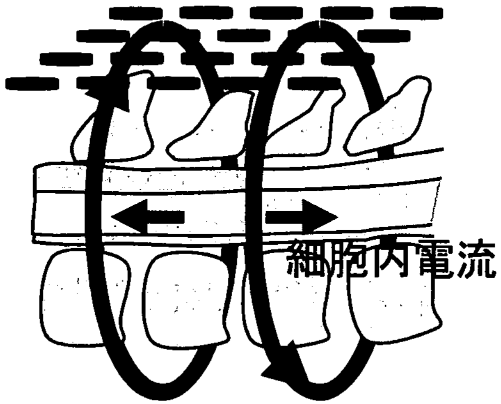
責任病巣を絞って最小侵襲で手術を行うために、神経機能評価のための検査法の開発が望まれる。

脊髄誘発磁界計測（1997～）

従来の電位計測よりも非侵襲的で、空間分解能に優れる
新しい脊髄機能診断法

電位計測　　vs　　磁界計測

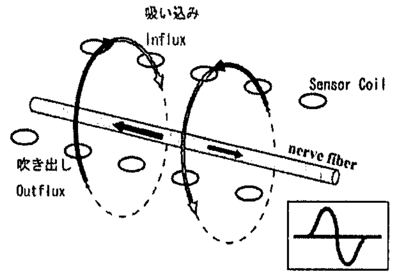




電流は脳脊髄液や軟部組織で拡散し、骨で減衰する。

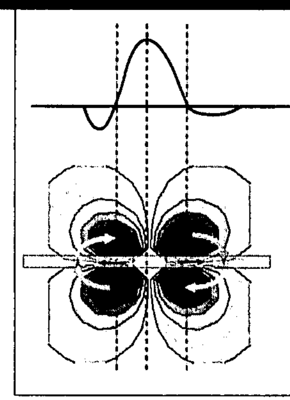
磁界は、周囲組織の影響を受けない。

[redacted]



磁界が横切るようにセンサーコイルを置き、磁界活動を測定する

[redacted]



活動電位

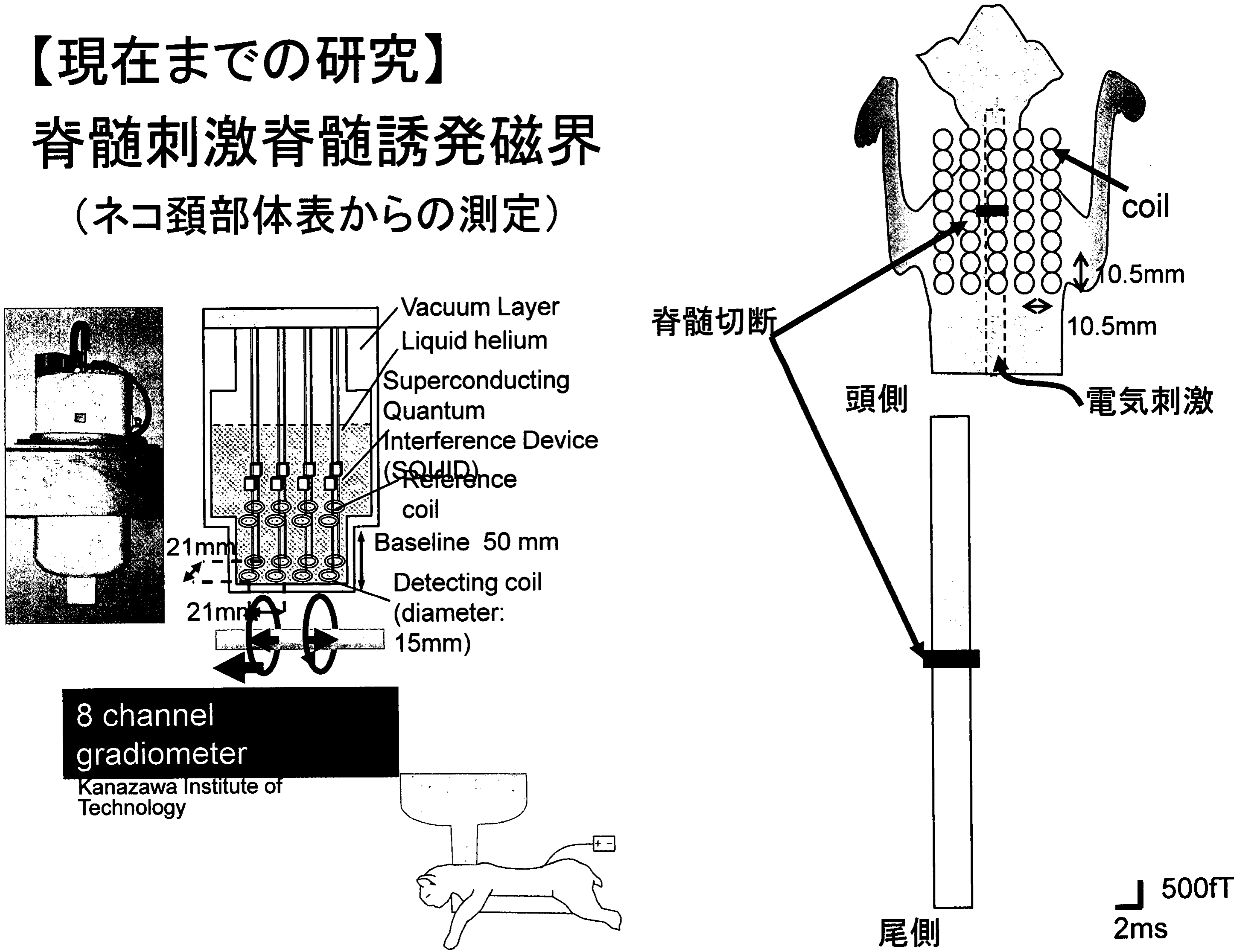
Magnetic contour map

伝導性神経活動は脱分極を中心とした四重極子として現わされる。

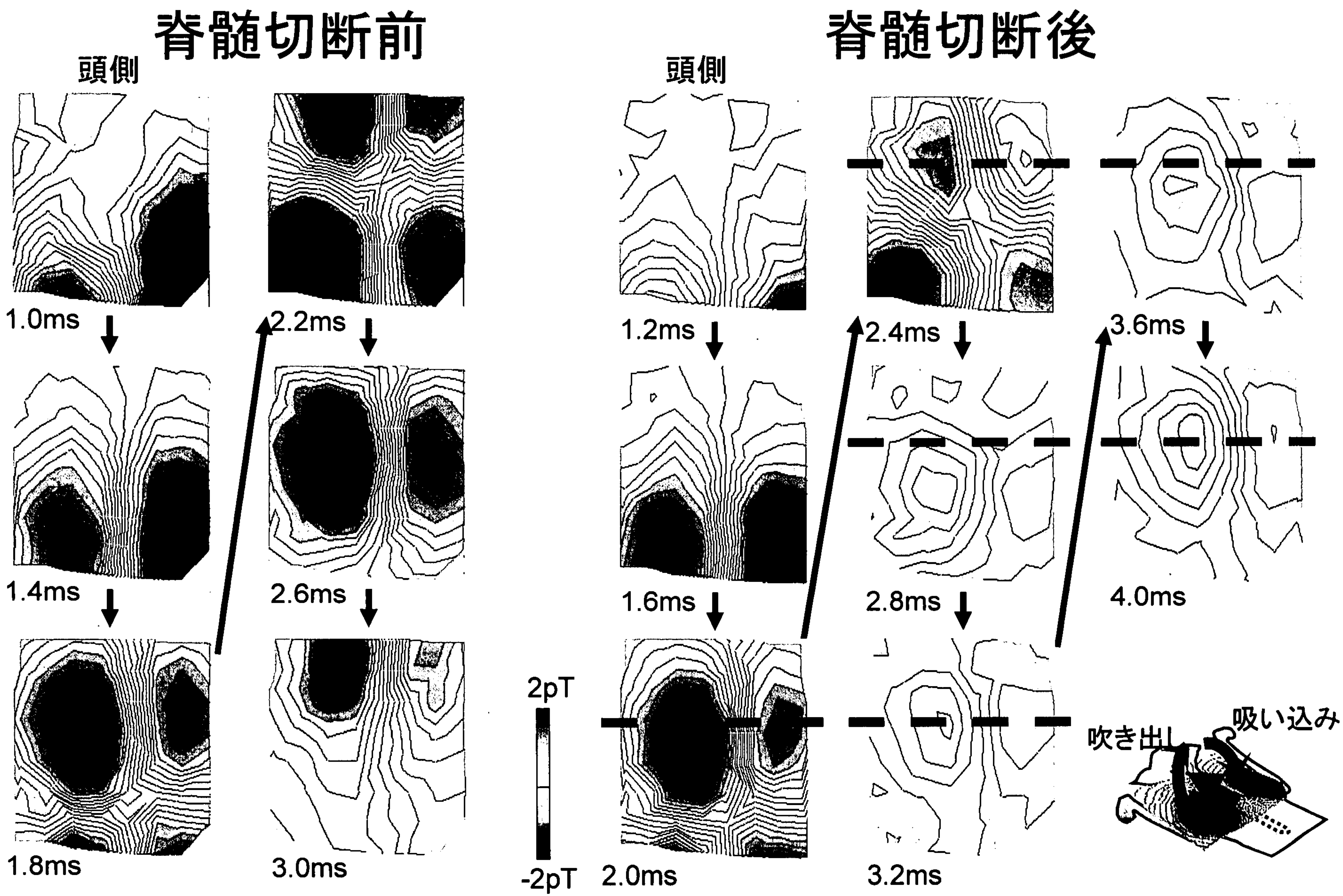
【現在までの研究】

脊髄刺激脊髄誘発磁界

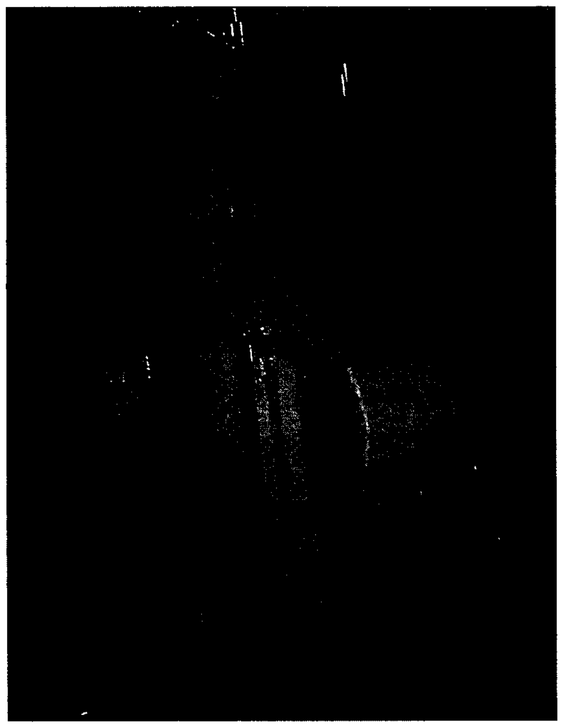
（ネコ頚部体表からの測定）



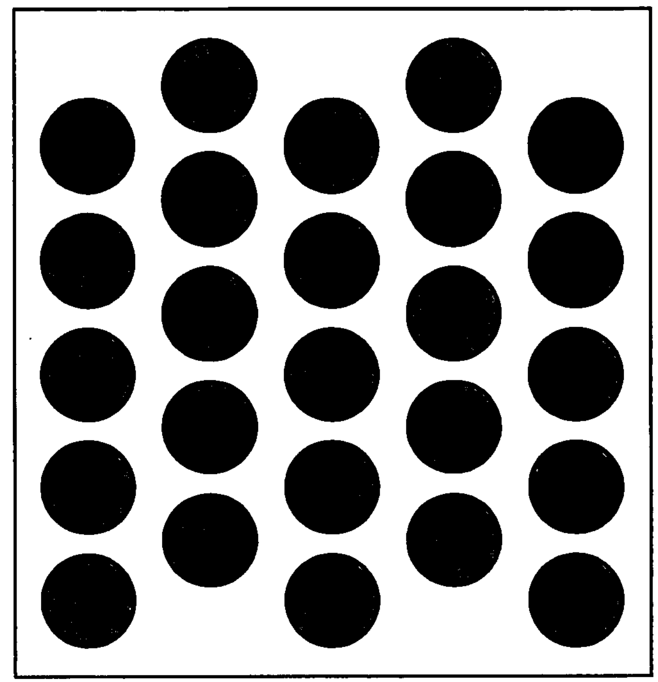
脊髄誘発磁界等磁場線図



臨床用脊髄用磁界測定装置

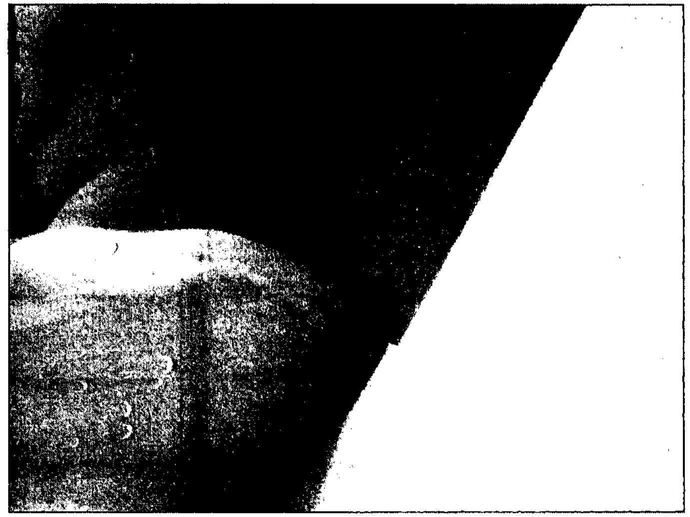


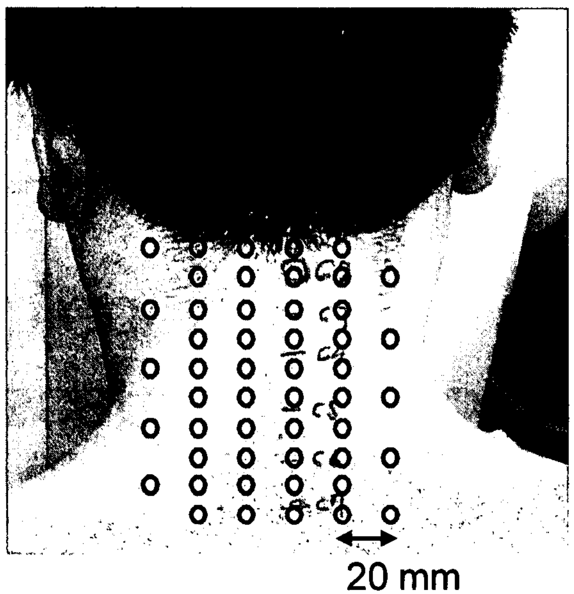
Sensor Layout

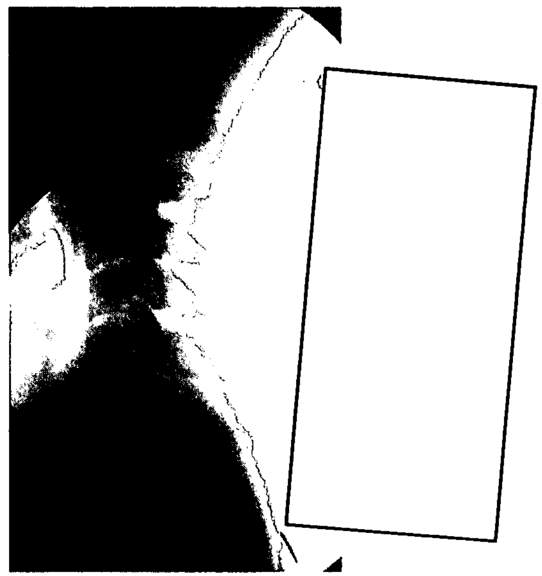


25 ch 脊髄磁界測定装置(金沢工業大学)

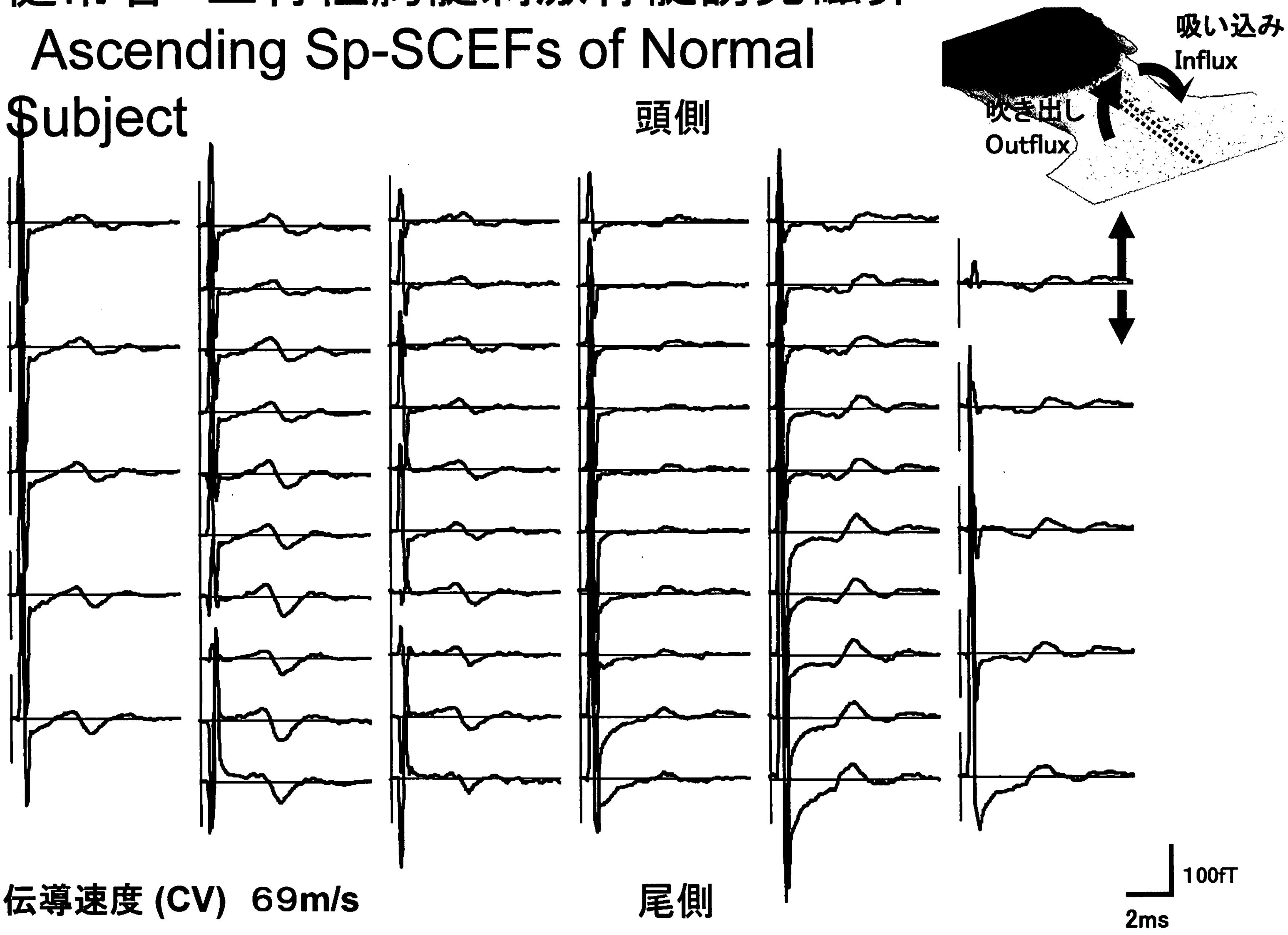
脊髄誘発磁界測定
Measurement of SCEFs





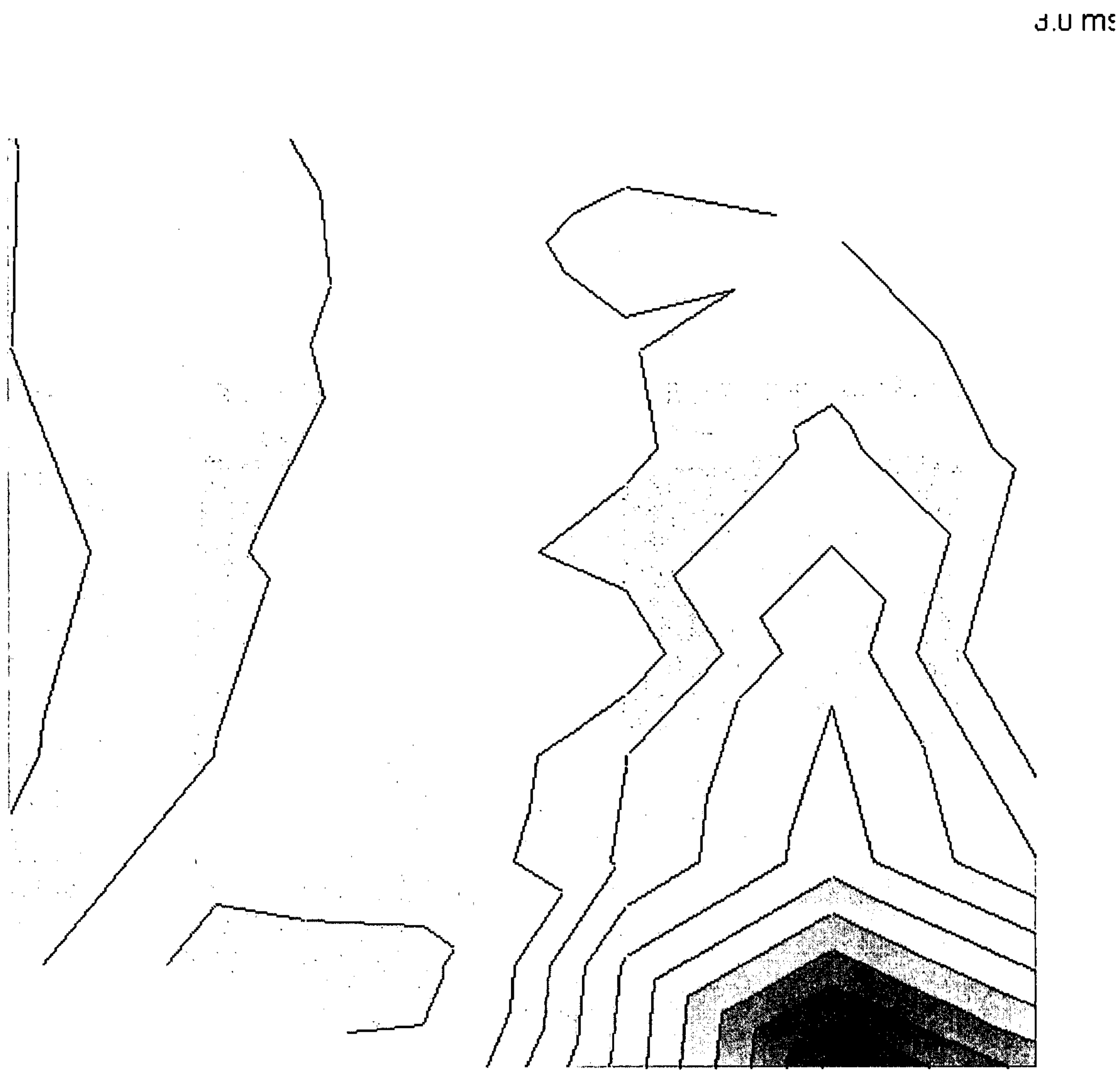


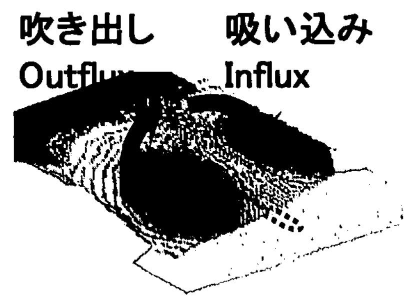
健常者　上行性胸髄刺激脊髄誘発磁界
Ascending Sp-SCEFs of Normal Subject

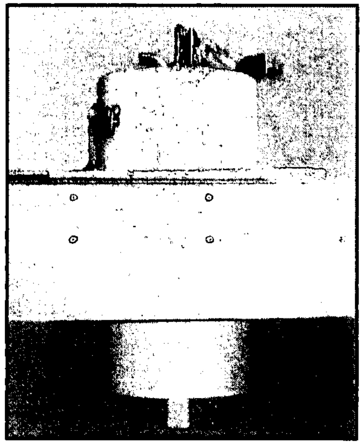


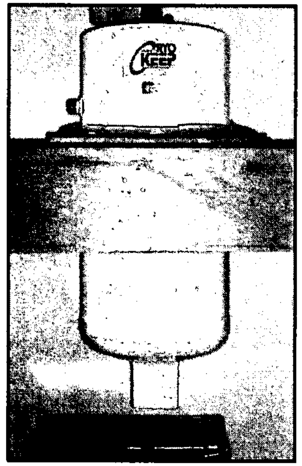
伝導速度 (CV)　69m/s

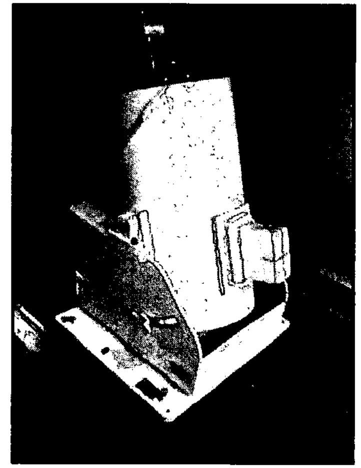
健常者　上行性胸髄刺激脊髄誘発磁界
Ascending Sp-SCEFs of Normal Subject

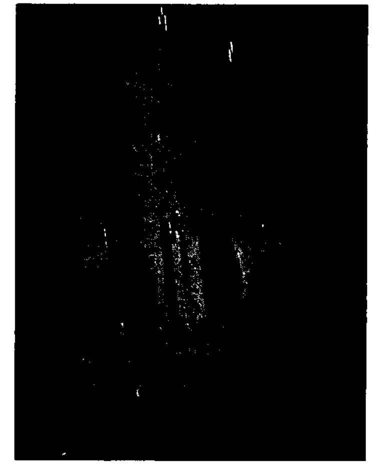




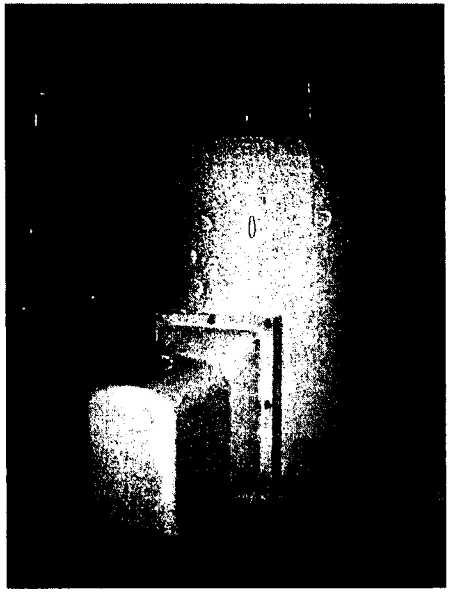

1999~
1 × 3 channel system


2000~
8 × 3 channel system


2004~
10 × 3 channel system

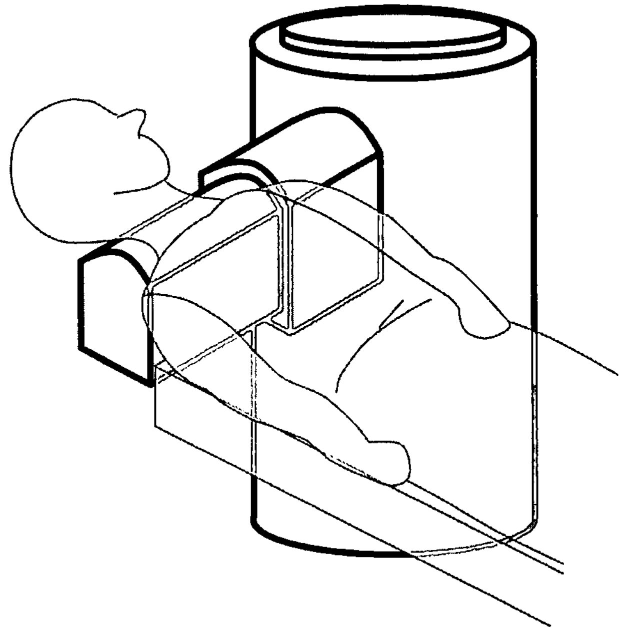

2005~
25 × 3 channel system

The sensor fits on cervical spine.



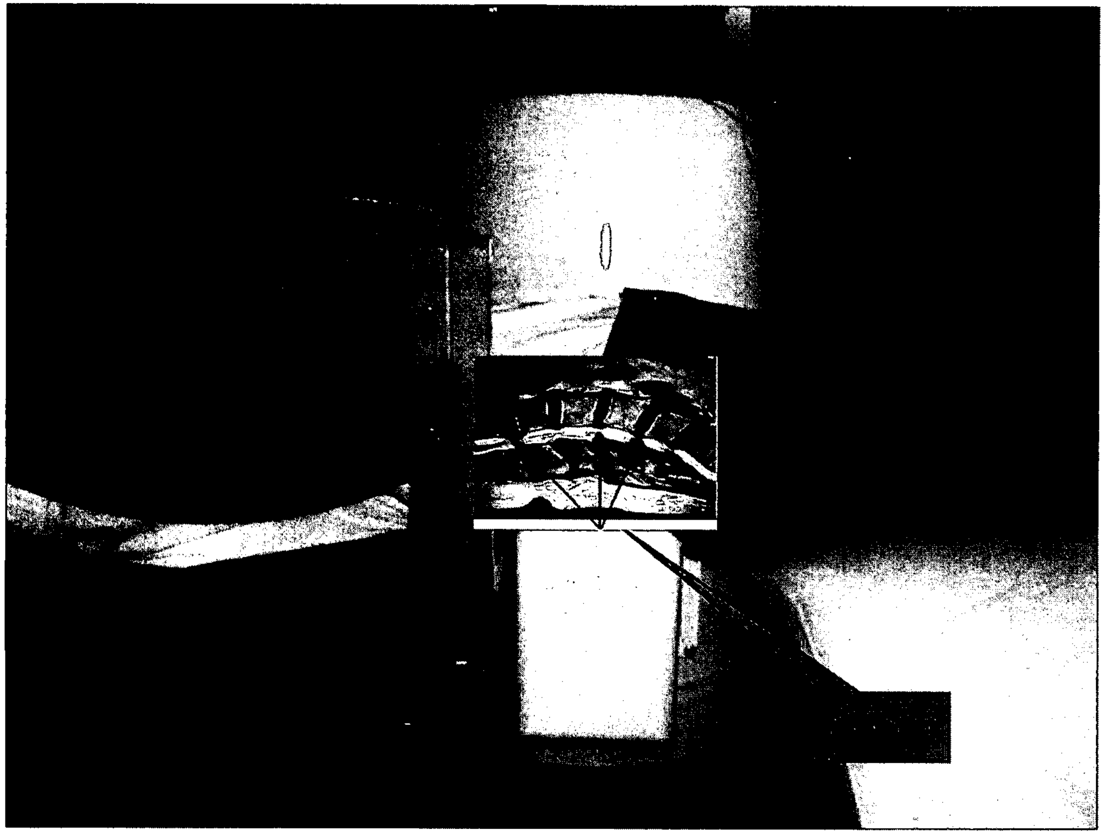
2007~

35×3 channel system



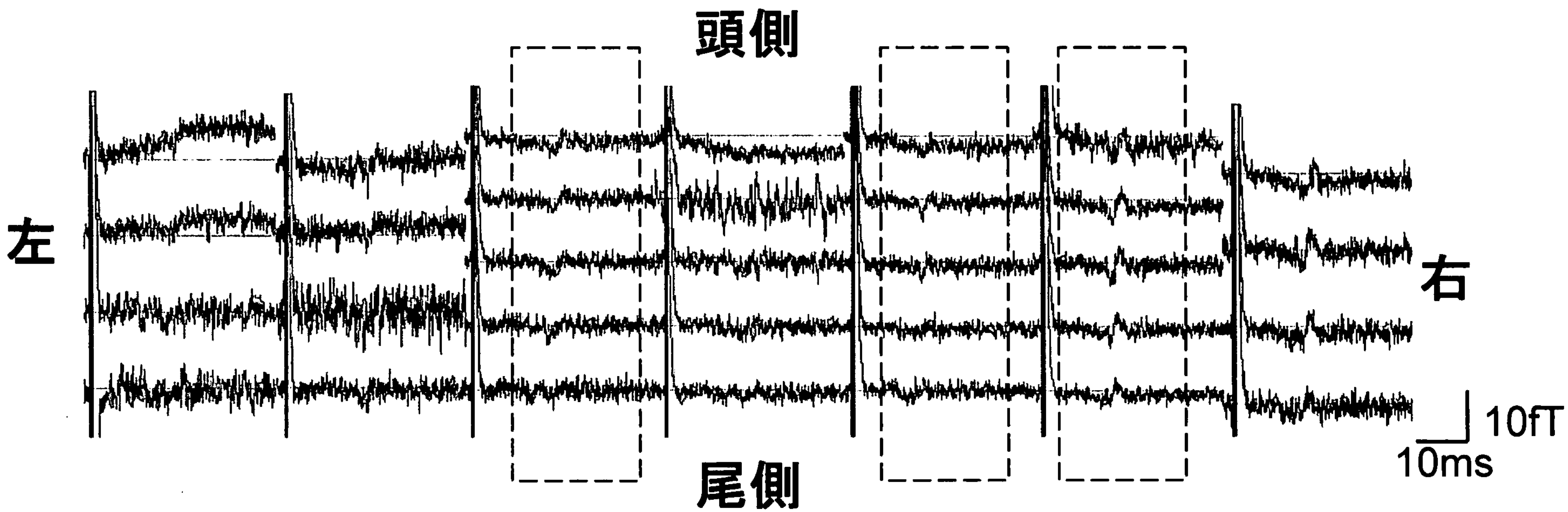
仰臥位測定のMerit

1、安静による筋磁図の影響排除、体動を最小限に制限。
2、自重によりセンサーと脊髄の距離短縮。



刺激
- 腓骨神経　@腓骨頭
- 0.5msec square pulse
- 5-7mA intensity
- 15Hz frequency

記録
- 500-5kHz Filtering
- 40,000kHz sampling
- 4000-6000 average



伝導速度　=100m/s

脊柱管内を上行する馬尾の活動電位をとらえた可能性が高い

様々な問題点

・刺激時の痛み対策
・低シグナル、高ノイズ⇒S/N比の向上
・測定時間の短縮

を改善することで馬尾の活動電位をとらえ、多椎間にわたる腰部脊柱管狭窄症の神経機能診断・障害レベル診断が可能になる可能性が高い。

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Clinical Neurophysiology xxx (2008) xxx–xxx

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Evaluation of segmental spinal cord evoked magnetic fields after sciatic nerve stimulation

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Accepted 14 January 2008

Abstract

Objective: We have previously reported that the measurement of spinal cord evoked magnetic fields (SCEFs) could be a helpful method for evaluating spinal cord function or detecting conduction blocks in the spinal cord. However, there have been no reports about segmental-SCEFs as a complex of axonal and synaptic activities in the spinal cord. The purpose of this study is to record and evaluate segmental-SCEFs.
Methods: The segmental-SCEFs were measured over the lumbar dural tubes of adult rabbits using our SQUID system following sciatic nerve stimulation; spinal cord evoked potentials (SCEPs) were also measured to compare the results.
Results: SCEPs showed conductive sharp waves following gentle waves, suggesting action potentials and synaptic potentials, respectively. The isomagnetic field maps of SCEFs showed a quadrupolar pattern propagating from the caudal to the cranial region within a short latency time, and after the conductive magnetic fields passed, stationary dipolar fields appeared and were sustained at some vertebral levels.
Conclusions: The quadrupolar magnetic fields were estimated to be generated from conducting action potentials, and the dipolar fields were thought to be caused by synaptic activities.
Significance: Through the measurement of segmental-SCEFs, the conductive neural and synaptic activities in the spinal cord can be visualized and distinguished. This is the first report to record and visualize the sequence of events ranging from the axonal activities of peripheral nerves and the spinal tract to the synaptic activities in the spinal cord.

Keywords: Synaptic activity; Spinal cord evoked potential; Spinal cord evoked magnetic field; Neuromagnetic recording; Sciatic nerve; Segmental-SCEF

1. Introduction

Pioneered in 1968, magnetoencephalography (MEG) (Cohen, 1968), which involves detecting magnetic fields produced by synaptic activities in the cortex, is already widely approved both for clinical use and for basic science research.

Compared with measurement of electric potentials, magnetic fields are less influenced by surrounding tissue and neuromagnetic recordings also have a theoretical advantage for spatial resolution (Trahms et al., 1989; Hashimoto et al., 1994; Mackert et al., 1997). We previously reported that spinal cord evoked magnetic fields (SCEFs) after spinal cord stimulation could be detected, and we were able to identify a conduction block at the site of a spinal cord lesion for the first time in an animal study (Kawabata et al., 2002). These signals are estimated to originate from neural conductive action potentials in the white matter of the spinal cord.

When considering spinal cord function, synaptic activities in the gray matter are as important as the neural conductive activities in the white matter. Because conductive neural activities in the white matter and synaptic activities

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in the gray matter are almost simultaneous and adjacent, it was thought to be difficult to separate the two types of neural activities by neuromagnetic recordings.

Though conductive neural activities from the peripheral nerve to the cauda equina or the synaptic activities of the spinal cord in humans have been previously reported by neuromagnetic recordings (Mackert et al., 1997, 2001a,b; Klein et al., 2006), there was no continuance between the two events. And there have been no detailed reports about a sequence which bridges the axonal activities of peripheral nerves and spinal tract with the synaptic activities in the spinal cord (segmental-SCEFs).

The purpose of this study was to record and evaluate segmental-SCEFs as a complex of axonal and synaptic activities, making a close comparison with the results of spinal cord evoked potential (SCEP) measurements in the same subjects.

2. Materials and methods

2.1. Materials and preparation

Eight rabbits (adult Japanese white, 2.5–3.0 kg) were used for these experiments. Initially, anesthesia was induced with ketamine chloride (25 mg/kg, i.m.) and medetomidine chloride (0.1 mg/kg, s.c.). An intravenous infusion of ketamine chloride (20 mg/kg/h), medetomidine chloride (0.1 mg/kg/h) and vecuronium bromide (0.3 mg/kg/h) was used to maintain a completely relaxed muscle condition. A tracheotomy was performed and ventilation was maintained by a tracheal tube on a respirator. The general conditions of the rabbits were monitored by using an electrocardiogram.

Lumbar laminectomy from L4 to L7 was carefully performed in order to expose the dural tube for measurements of SCEPs. Bilateral sciatic nerves were also exposed for stimulation at the mid-thigh by a posterior approach.

2.2. Positioning for the measurements

The rabbits were placed prone on an *X–Y–Z* coordinate stage; the lumbar dural tubes were placed on the horizontal *X–Y* plane directed in parallel with the *Y*-axis.

2.3. Stimulation

Electrical stimuli (square wave pulses, 0.03 ms in duration, 5–8 mA in intensity) were applied to the sciatic nerve of one side just above its bifurcation using a bipolar electrode, MEB2200 (Nihon Koden, Japan). The frequency of the stimulation was designed using different conditions (10 Hz and 60 Hz) to examine the effect of synaptic fatigue.

2.4. Measurements

2.4.1. SCEP (spinal cord evoked potential)

SCEPs were recorded to compare the result with that of segmental-SCEFs, under the same stimulating conditions, at several points spaced 10 mm apart along the median of the exposed dural tube. SCEPs were measured by bipolar recordings such that a reference electrode was placed at 5 mm cranially on the dural tube (Fig. 1a). Fifty to 100 trials were averaged at each point, and the signals were acquired with 10 Hz to 5 kHz band pass filtering.

2.4.2. SCEF (spinal cord evoked magnetic field)

Magnetic recordings were taken with an 8-channel SQUID (Superconducting Quantum Interference Devices) system (Kanazawa Institute of Technology, Japan) in a magnetically shielded room (Adachi et al., 2006). Each channel was arranged in a 2×4 parallel configuration (with a 21 mm distance between neighboring channel positions). The baseline between the pick-up coils and the reference coils was 50 mm, and each pick-up coil was 15 mm in diameter (Fig. 1b).

For all magnetic recordings, the dewar bottom was placed on a plane about 5 mm over the lumbar dural tube. A rectangular measurement grid was obtained by moving the dewar sequentially on the same plane. Each measurement point was spaced 10.5 mm apart along the *X*-axis and 7 mm apart along the *Y*-axis, and all SCEFs were measured at about 96 different points (Fig. 1c). Approximately 3000 trials were averaged at each position, and the signals were acquired at a sampling rate of 40 kHz, with 10 Hz to 5 kHz analog band pass filtering.

2.5. Estimation of current sources

The minimum-norm estimation as a spatial filtering method, a popular method for estimating the current distribution in the human brain from magnetic field measurement (MEG) without detailed information about the generator profile, was adopted to estimate the current sources from the obtained data in technical cooperation with Tokyo Metropolitan University (Iwaki and Ueno, 1998; Sekihara et al., 2001, 2005, 2006; Matsuura and Okabe, 1995). Estimated current sources were visualized and referred to the X-ray image to match the localization of the spine and the spinal cord.

After the study, the animals were euthanized by intravenous infusion of pentobarbital (120 mg/kg). The study method was approved by the Ethical Committee of Tokyo Medical and Dental University.

3. Results

3.1. SCEPs after stimulation to the sciatic nerve

In all subjects, SCEPs after sciatic nerve stimulation could be recorded successfully.

SCEPs consisted of conductive polyphasic spike waves (E1) followed by gentle waves. The polyphasic wave propagated from the caudal to the cranial region at a conduction velocity of 60–90 m/s; those waves gradually decreased their amplitude toward cranial region (Fig. 2a).

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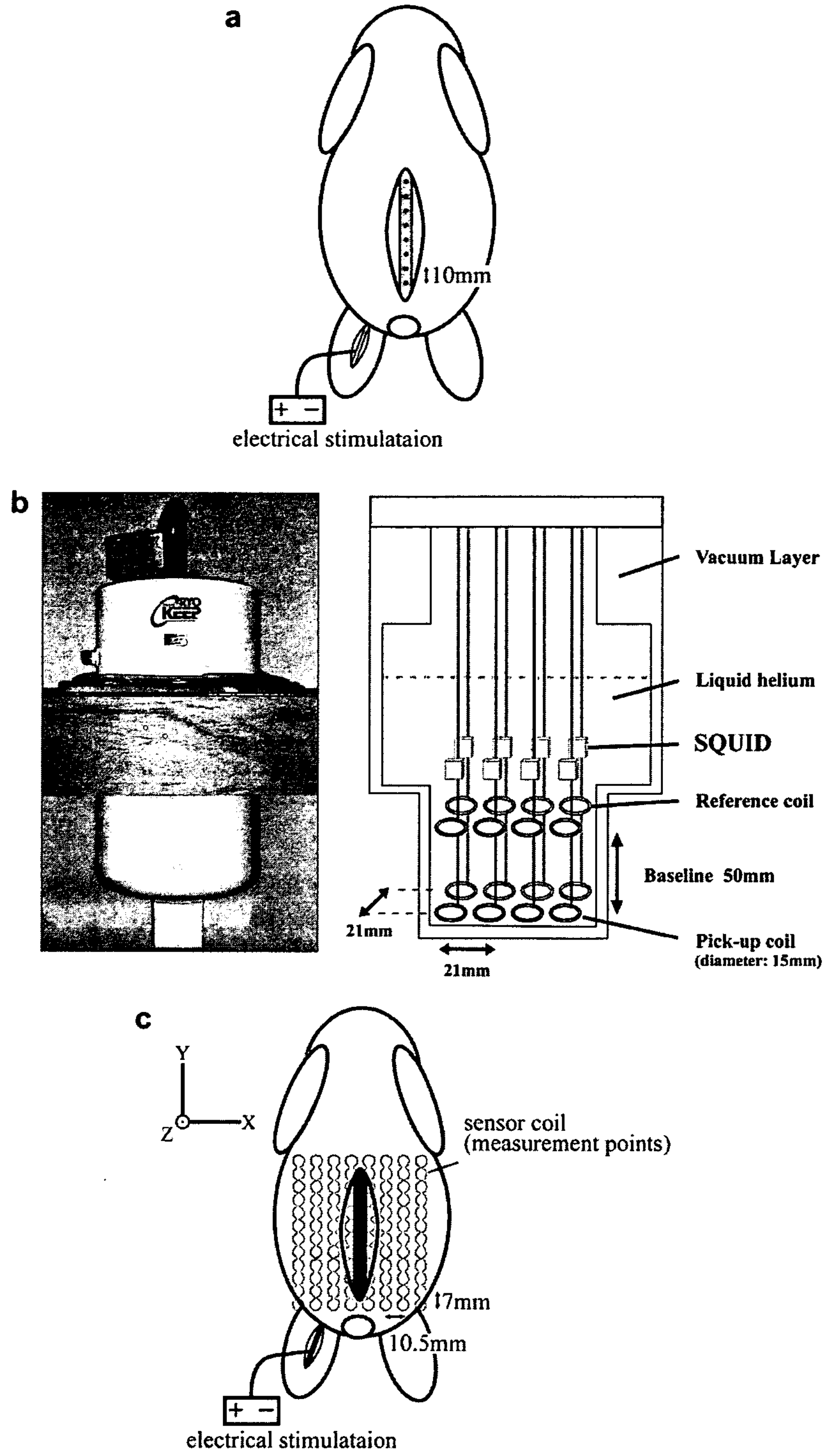

Fig. 1. (a) SCEPs were recorded along the median of the exposed spinal cord after laminectomy by bipolar recording. Each measurement point was spaced 10 mm apart. (b) Our 8-channel SQUID system: subjects were positioned prone just below the dewar on an *X–Y–Z* ordinate stage. Orthogonal elements to the measurement plane of evoked magnetic fields generated around the nerve were able to be detected by pick-up coils. (c) SCEFs were measured over the lumbar spinal cord at about 96 different points (circles) after the electrical stimulation to the sciatic nerve.

The gentle waves (E2) recorded largely around the L6 vertebral level (and not observed above the L4 vertebral level) did not propagate along the spinal cord. The amplitude of E2 decreased when the frequency of the stimulation was increased from 10–60 Hz, whereas the waveform of E1 did not change (Fig. 2b).

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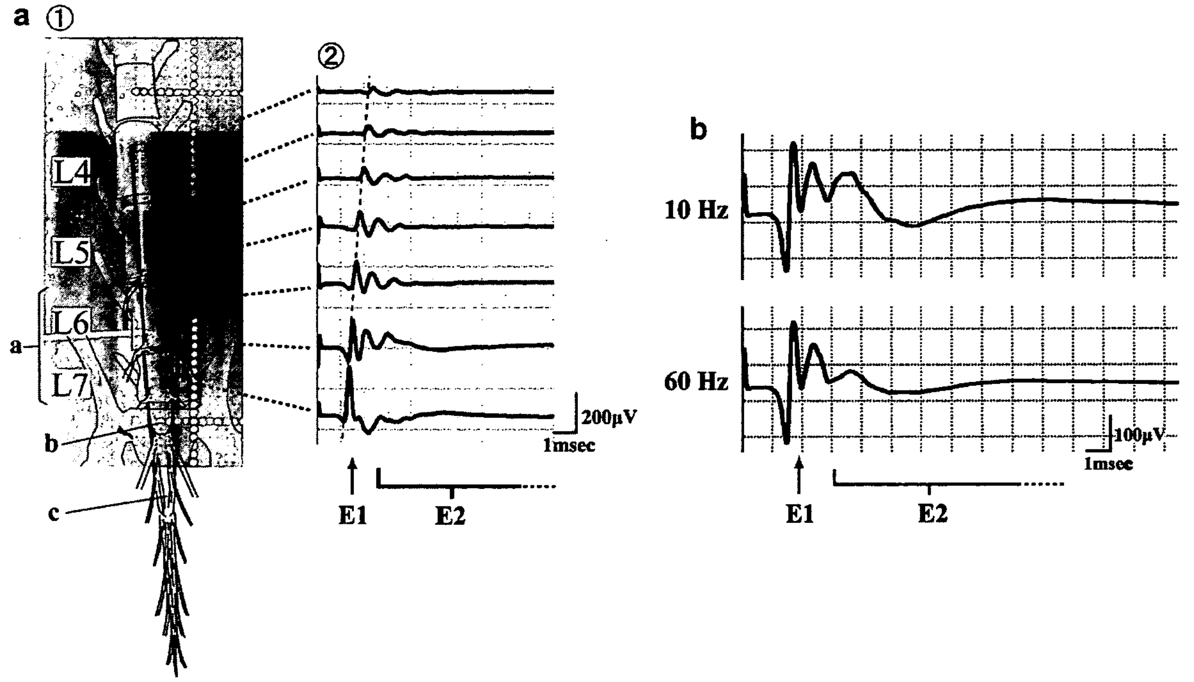

Fig. 2. (a) ① Anterior–posterior view of X-ray image and schematic representation of spinal cord and nerve roots in the lumbosacral spine of rabbit. a, Lumbar enlargement; b, conus medullaris; c, cauda equina. ② SCEPs recorded after sciatic nerve stimulation. E1, conductive polyphasic spike waves; E2, static gentle waves. The polyphasic spike waves propagated toward the cranial region, and later gentle waves were recorded. The largest was noted around the L6 vertebral level, and did not show propagation along the spinal cord. (b) Waveforms of SCEPs at the L6 vertebral level; the amplitude of E2 decreased under high frequency stimuli, whereas E1 did not change its waveform.

3.2. SCEFs after stimulation to the sciatic nerve

In all subjects, SCEFs after sciatic nerve stimulation could also be recorded.

Fig. 3a shows one of the results of the waveform arrangement of the SCEF after left sciatic nerve stimulation based on the measurement points. The signal above the baseline indicates outflux magnetic flow from ventral to dorsal, and the signal below the baseline indicates influx magnetic flow from dorsal to ventral.

Obtained magnetic fields also consisted of polyphasic spike waves (M1) and the following gentle waves. The spike waves showed biphasic configurations; the first deflection of the magnetic signals at the left side of the spinal cord was directed outward, and that of the right side was directed inward. The polarity reversed for the second deflection. Those waves propagated to the cranial region at a conduction velocity of 60–100 m/s.

The following gentle waves (M2), characterized by low amplitude and long duration, were recorded as the largest at about the L6 vertebral level. The amplitude of these waves decreased when high frequency stimuli were applied to the sciatic nerve (Fig. 3b).

The isomagnetic field maps of SCEFs (Fig. 4a) showed a quadrupolar pattern, and these quadrupolar fields propagated from the caudal to the cranial region with a short latency time. Just after this leading magnetic field passed, at least four dipolar fields emerged one by one. At first, a dipolar field appeared at about the L6 vertebral level; the next emerged at about the L5 vertebral level instead of the disappearance of the first dipolar field. Subsequently, the third arose at about the L4 level instead of the disappearance of the second field. After the third dipolar field disappeared, the last one emerged and was sustained for a long duration at the same position as the first. Each dipolar field emerged and disappeared at the same position on the spinal cord without propagation. The direction of the assumed current distribution of each dipolar field looked upward cranially or downward caudally, without uniformity. However, the first and the last fields were in the same direction.

3.3. Estimated current sources

The current sources estimated by the minimum-norm method were visualized and matched to the X-ray image (Fig. 4b). Small arrows indicated the current direction, and the color density in the map indicated the current intensity. A conducting forward and backward current flow, according to the pathway from the nerve roots to the spinal cord, was recognized within a short latency time. Furthermore, volume currents surrounding the intra-axonal currents were also observed. In addition, some stationary currents in turn emerged and disappeared at the different segments one by one. These stationary currents

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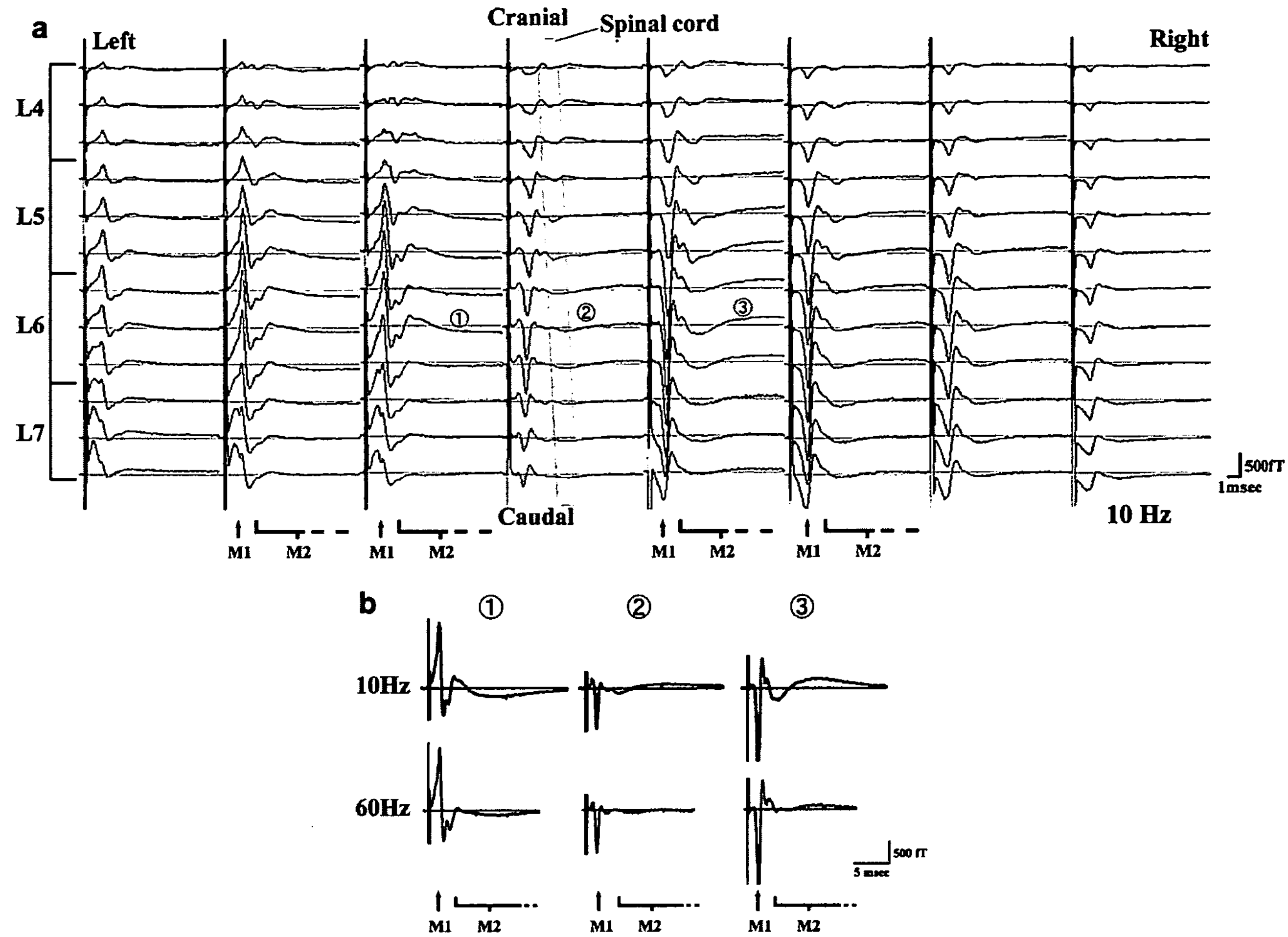

Fig. 3. (a) The waveform arrangement of SCEFs after left sciatic nerve stimulation (10 Hz) based on the measurement points. The gray bar indicates the location of the spinal cord. Some waves consisted of polyphasic spike waves (M1) followed by gentle waves (M2). (b) Some waves were selected to compare the results between 10 Hz and 60 Hz stimulation at the same points in the same subject. The numbers indicate the positions of the waves in (a). The gentle waves (M2) decreased their amplitude, whereas the spike waves (M1) did not change their waveforms under high frequency stimuli.

corresponded to the dipolar fields in the isomagnetic contour map.

4. Discussion

We had previously reported that magnetic fields which were evoked from the spinal cord or peripheral nerve were measurable using our SQUID system, where conductive action potentials were represented as a quadrupolar isomagnetic field pattern and the depolarization corresponded to the center of the quadrupolar fields (Okubo et al., 2003; Fukuoka et al., 2002, 2004).

In this study, we measured magnetic fields around the lumbar spinal cord evoked following sciatic nerve stimulation in order to record and evaluate not only conductive axonal currents but also segmental synaptic activities in the spinal cord.

After electrical stimuli were applied to the sciatic nerve of the rabbit, axonal currents propagated along the nerve and diverged to the L6–S2 nerve roots in the lumbosacral plexus (Barone et al., 1973). Some axonal impulses, after flowing into the spinal cord, would climb up the ascending tracts in the dorsal column to the cranial region and some impulses would switch the axons by synaptic transmission in the dorsal horn and climb up the ipsilateral or contralateral ascending fibers in the white matter. Regrettably, physiological and electrophysiological detailed analysis of the dorsal horn or root potentials of the rabbit were not found in the literature, however, we assumed the constitution of the spinal cord of rabbit was similar to that of cats or rats (Bernhard, 1953; Eccles et al., 1962; Shimoji et al., 1977; Patrick and Malcolm, 1997).

In the segmental-SCEPs, after peripheral nerve stimulation, two different types of potentials could usually be recorded – the spike wave in the short latency followed by gentle and long lasting waves. The spike wave was thought to be derived from the action potentials of the primary afferent of the nerve root and the axonal currents in the white matter, and the following gentle waves originated from synaptic activities in the gray matter of the spinal

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Fig. 4. (a) The isomagnetic field maps of SCEFs; the red color indicates outflux magnetic flow from ventral to dorsal, and the blue color indicates influx magnetic flow from dorsal to ventral. A quadrupolar magnetic field propagated from caudal to cranial within a short latency time (0.8–2.3 ms) almost according to the neural pathway. Just after the quadrupolar magnetic field passed, some stationary and sustained dipolar fields emerged and faded away at a different segment. Initially, one dipolar field emerged at the L6 level (black arrows), the next one appeared at the L5 level (red) in turn; the third one emerged at the L4 level (green), and the last one appeared again at the L6 level (black). (b) Estimated current sources. Propagating intra-axonal currents, forward (white arrows) and backward (gray arrows) current flows and volume currents (surrounding small black arrows) were recognized within a short latency time (0.8–2.3 ms). After the propagating currents, some stationary and sustained currents emerged and faded away at the different segments one by one. Initially, one current source emerged at the L6 level (black arrows), the next one appeared at the L5 level (red), the third emerged at the L4 level (green), and the last one appeared again at the L6 level (black).

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