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# Omental Transposition Decreases Ischemic Brain Damage Examined in a New Ischemia Model

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**Key Words**

Cerebral ischemia · Omental transposition · Single photon emission computed tomography · Magnetic resonance imaging · Experimental model

**Abstract**

***Purpose:*** The aim of this study was to determine whether omental transposition at the time of focal cerebral ischemia can decrease ischemic brain damage produced in dogs, in a new ischemia model, which had been described by us. ***Methods:*** In group 1 (n = 5), the left internal carotid artery and arterial circle of the brain (posterior communicating artery in humans) were occluded permanently. In group 2 (n = 5), additionally to this ischemia model, omental transposition was performed simultaneously. In the postoperative early period (first 24 h), single photon emission computed tomography (SPECT) and in the late period (72–96 h) SPECT and magnetic resonance imaging (MRI) of the brain were performed. Mann-Whitney U, paired t and Wilcoxon signed rank tests were used for statistical analyses, and $p < 0.05$ was considered significant. ***Results:*** The dogs had a neurological score (NS) of 3.6 ± 0.5 and 3.4 ± 0.5 in groups 1 and 2, respectively, in the early period ($p > 0.05$). In the late period, the dogs had an NS of 4.4 ± 0.5 and 5.6 ± 0.5 in groups 1 and 2, respectively ($p < 0.05$). The NS of each group differed significantly between the early and late period ($p < 0.05$). Early SPECT imaging showed 50 ± 7.0% and 52 ± 8.4% hypoperfusion corresponding to the left middle cerebral artery territory in groups 1 and 2, respectively ($p > 0.05$). In the late period, the degree of hypoperfusion decreased to 34 ± 5.5% and 12 ± 4.8% in groups 1 and 2, respectively ($p < 0.05$). The degree of hypoperfusion in both groups changed significantly between the early and late period ($p < 0.05$). In $T_1$- and $T_2$-weighted MRI images, the volume of the lesion in group 1 was significantly greater than in group 2 ($p < 0.001$). ***Conclusion:*** In our new ischemia model, simultaneous omental transposition is helpful in reversing the neurologic deficit and cerebral ischemic damage.



## Introduction

Omentun is an organ that has the ability of neovascularization beside other features, such as absorption, secretion, regeneration and adhesion [1, 2]. Goldsmith et al. [3] were the first to use the omentum in cerebral revascularization in 1973, demonstrating in dogs that the intact omentum placed over the cortex developed a collateral

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circulation to the brain. Yonekawa and Yaşargil [4] reported similar results in 1974, using an omental free flap microsurgically anastomosed to the superficial temporal artery and vein. Subsequent experimental works showed that the placement of the omentum on the rabbit, dog and monkey brain prior to middle cerebral artery (MCA) ligation protected the animals from cerebral infarction, compared with control animals without omental protection [5–9]. However, omental placement on the brain simultaneous with MCA occlusion inducing infarction was ineffective [8].

The data obtained from these animal experiments suggested that omental transposition to the human brain might be a prophylactic procedure. Elimination of transient ischemic attacks has already been reported [10–12]. Although it was not supported by animal experiments, omental transposition was considered as a therapeutic procedure for patients with completed stroke and stabilized neurological deficits, and some clinical improvements in motor and speech function have been reported [13–16]. However, Herald et al. [17] have been unable to reproduce these findings. Therefore, we planned an animal experiment using a new experimental ischemia model in order to support these clinical findings.

## Methods

The animals were cared for in accordance with the National Institute's guide for the care and use of laboratory animals. These protocols were reviewed and approved by the animal use committee.

Ten adult male mongrel dogs, weighing 16–21 kg, were premedicated with ketamine 10 mg/kg and xylazine hydrochloride 2 mg/kg intramuscularly. Anesthesia was induced with a bolus of intravenous propofol (2 mg/kg). Endotracheal intubation was performed without a neuromuscular relaxant, and the animals were ventilated with oxygen ($FiO_2$: 1.0). Total intravenous anesthesia with propofol (6 mg/kg/h) and fentanyl (2 μg/kg) was used for maintenance. Noninvasive mean arterial pressure, end-tidal $CO_2$ ($PETCO_2$), electrocardiogram and oxygen saturation were monitored with a Criticare Poet-II (USA). The $PETCO_2$ was kept between 35–40 mm Hg. 0.9% NaCl was given (5 ml/kg/h) during the operation.

In all dogs, a linear incision was made in the left temporoparietal area between the midline and the orbitozygomatic line. This incision was carried down to the skull with all overlying soft tissue being completely removed from the bone. A 4 × 4 craniotomy was made and the dura was opened as wide as the craniotomy. The brain was lifted and displaced from the base of the skull. Then, following cisternal dissection, the internal cerebral artery (ICA), rostral cerebral artery (RCA; corresponding to the anterior cerebral artery in humans), MCA and arterial circle of the brain (ACB; corresponding to the posterior communicating artery in humans) [18] were exposed with the use of an operation microscope. After this procedure, the dogs were divided randomly into two groups. In group 1 (n = 5), the ACB and ICA were transected (fig. 1) after bipolar coagulation, proximal to the origin of the ACB. The dura was then hanged with several sutures to the calvarium in order to prevent epidural hemorrhage, and a thin layer of spongostan was laid over the cortex leaving the dura open. This was followed by closure of the soft tissues overlying the dura. In group 1 (n = 5), laparotomy and splenectomy without omental transposition were also performed in order to standardize the treatment. In group 2 (n = 5), the preparation and lengthening of the omentum under the scalp was performed as described by Goldsmith et al. [3], with little modification. Laparotomy was done through a midline incision, following which the omentum was extensively lengthened. This was accomplished by removing the omentum directly from its junction with the spleen, which required splenectomy, and from its middle and distal attachment to the greater curvature of the stomach. The vascular supply to the omentum was maintained mainly by the splenic artery. After the omentum had been lengthened, transverse skin incisions were made along the chest, shoulder and neck, which were undermined and connected to form a subcutaneous tunnel, approximately 4–5 cm in width and then brought to the temporoparietal area subcutaneously. The pedicled omentum was laid on the underlying brain and secured by several sutures to the cut edge of the dura. In order to prevent tension on the omentum when the skin was closed, the temporal muscle and fascia overlying the omentum was loosely closed (fig. 2).

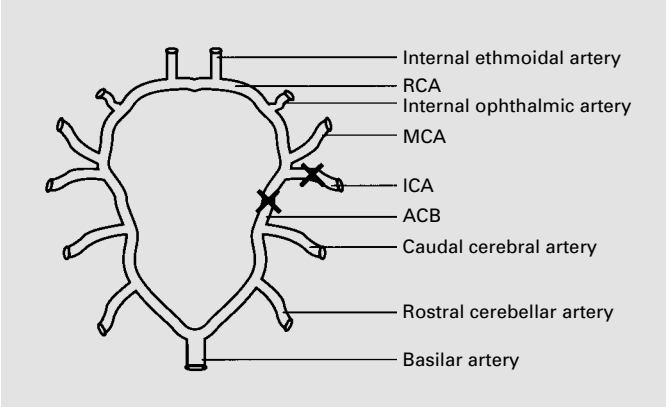



**Fig. 1.** Schematic representation of cerebral arteries in dogs. The transected arteries are shown with an X.

After the operation, the dogs were extubated and allowed to breathe room air spontaneously, and they were observed until recovery from anesthesia. During the first 4 postoperative days, the animals received daily injections of 0.5 g ceftriaxone and were fed by a routine diet following surgery.

In the early (first 24 h) and late (72–96 h) postoperative periods, all the dogs were anesthetized with 2 mg/kg intramuscular xylazine, 0.15 mg/kg midazolam and 2 mg/kg ketamine intravenously. Spontaneous breathing was continued. Then, in the early period, only brain single photon emission computed tomography (SPECT) imaging and in the late period both SPECT and cranial magnetic resonance imaging (MRI) methods were performed.

The neurological assessment was performed immediately before the early SPECT and late MRI and SPECT. The neurological status was scored from 1 to 6 as follows: (1) the dog could not move its legs on one side; (2) the dog could not stand up, but could move its legs

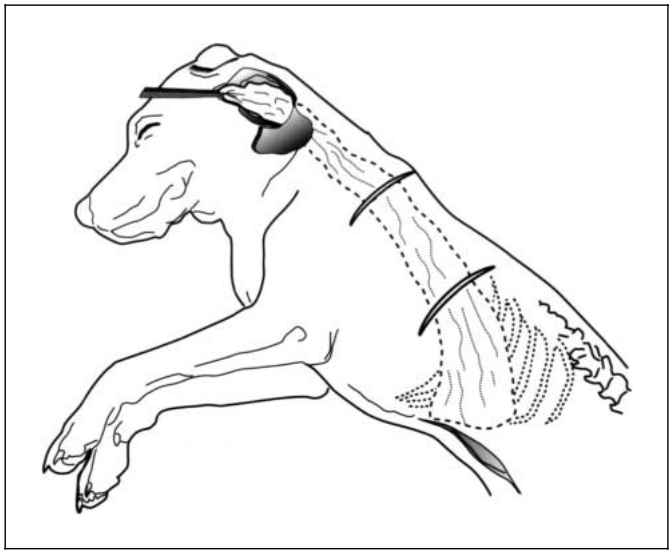


**Fig. 2.** Placement of the omentum in a subcutaneous tunnel along the chest and neck, the omentum being mobilized to cranial defect.

slowly on the paretic side; (3) the dog could stand up, but within 10 min fell to the paretic side; (4) the dog could stand up, but had difficulty in walking; (5) the dog could walk, but had difficulty in running, and (6) normal.

*SPECT Study*

$^{99m}$Tc-hexamethylpropylene amine oxime was used as a tracer (Ceretec; Amersham International, Little Chalfont, UK). A dose of 15 MBq/kg was injected intravenously. Within 30 min, high-resolution SPECT acquisition was performed with a single head Picker PRISM 1500 camera (Picker International, Cleveland Heights, Ohio, USA) with a high-resolution collimator. A full 360° rotation was acquired (60 frames × 6°, each for 35 s) with a matrix of 128 × 128. Six-millimeter-thick axial slices tilted along the orbitomeatal line were reconstructed by filtered back projection and corrected for attenuation. The imaging resolution was 8–9 mm. Transverse, sagittal and coronal sections were reconstructed. Perfusion defects were evaluated visually and semiquantitatively by color uptake scala. Counts/pixel ratios were divided into 10 different colors, each showing 10% bend from 0 to 100. A change in perfusion degree was calculated by comparing the values in the left and right (ipsilateral and contralateral) hemispheres of the individual range of interest. A threshold of 'lower than 60% of maximal cortical counts' was used in defining significant hypoperfusion in the SPECT images and the hypoperfusion degree at the center of the hypoperfused area was accepted as the degree of hypoperfusion.

*MRI Study*

Each dog underwent MRI with a 1.5-tesla scanner (MR-Edge, Picker, Cleveland, USA). $T_1$- and $T_2$-weighted (T1 W and T2 W) images (slice-slice interval 3 mm) were obtained in axial and coronal sections. Analysis of lesion volume was performed on a UNIX workstation (HP 9000/750) using an image analysis package (Analyze, Mayo Foundation, Rochester, Minn., USA). For each slice, the lesion area was determined by the region growing from one or more manually placed seed points. Manual editing of limits was performed when necessary. The lesion volume was calculated by multiplying the areas with the total slice thickness (plus correction for slice gap). For T2 W images, only areas that appeared hyperintense and for T1 W images, only areas that appeared hypointense on the scans in all three dimensions were defined as a lesion [19].

**Table 1.** Hemodynamic and respiratory parameters in both groups (mean ± SD)

| Parameters | Group 1 | Group 2 | p value |
|---|---|---|---|
| HR, beats/min | | | |
| Baseline (after anesthesia) | 138.6 ± 6.4 | 138.0 ± 11.0 | n.s. |
| After producing ischemia | 145.2 ± 7.2 | 146.6 ± 11.9 | n.s. |
| End of operation | 135.2 ± 6.0 | 136.6 ± 12.5 | n.s. |
| MAP, mm Hg | | | |
| Baseline (after anesthesia) | 82.8 ± 5.6 | 82.4 ± 5.5 | n.s. |
| After producing ischemia | 92.0 ± 6.5 | 89.6 ± 7.1 | n.s. |
| End of operation | 77.0 ± 5.7 | 76.8 ± 4.6 | n.s. |
| $SpO_2$, % | | | |
| Baseline (after anesthesia) | 97.0 ± 0.7 | 96.4 ± 1.1 | n.s. |
| After producing ischemia | 98.4 ± 0.5 | 98.2 ± 0.8 | n.s. |
| End of operation | 98.4 ± 0.5 | 98.0 ± 0.0 | n.s. |
| $ETCO_2$, mm Hg | | | |
| Baseline (after anesthesia) | 42.2 ± 1.4 | 43.4 ± 1.8 | n.s. |
| After producing ischemia | 35.4 ± 2.0 | 35.0 ± 1.0 | n.s. |
| End of operation | 35.4 ± 0.8 | 36.4 ± 1.1 | n.s. |

Group 1: untreated group; group 2: treated group with omental transposition. HR = Heart rate; MAP = mean arterial pressure; $SpO_2$ = oxygen saturation; n.s. = nonsignificant.

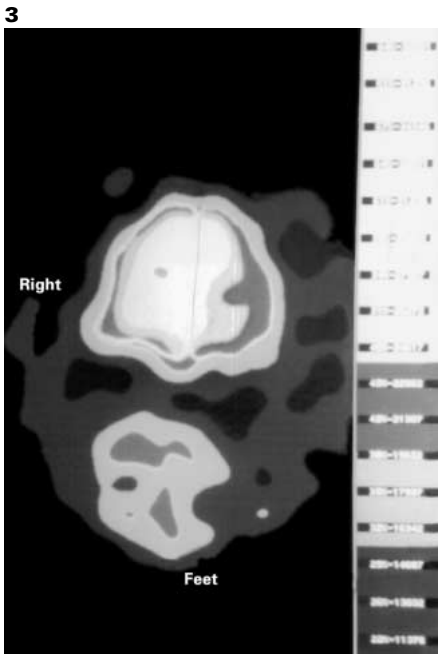
**Table 2.** NS and hypoperfusion degrees in brain SPECT images in both groups (mean ± SD)

| | Group 1 (n = 5) | Group 2 (n = 5) | p value |
|---|---|---|---|
| Neurological Score | | | |
| Early period | 3.6 ± 0.5 | 3.4 ± 0.5 | >0.05 |
| Late period | 4.4 ± 0.5[b] | 5.6 ± 0.5[a, b] | 0.020 |
| p (within group) | 0.046 | 0.034 | |
| Hypoperfusion degree, % | | | |
| Early period | 50 ± 7.0 | 52 ± 8.4 | >0.05 |
| Late period | 34 ± 5.5[b] | 12 ± 4.8[a, b] | 0.002 |
| p (within group) | 0.000 | 0.000 | |

Group 1: untreated group; group 2: treated group with omental transposition.

[a] Significant vs. group 1.

[b] Significant vs. early period.



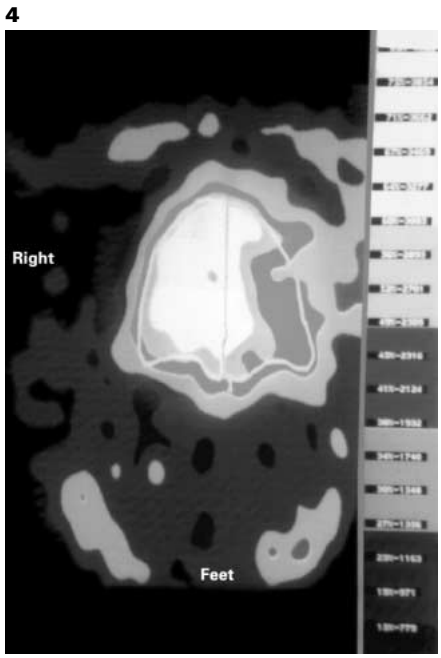
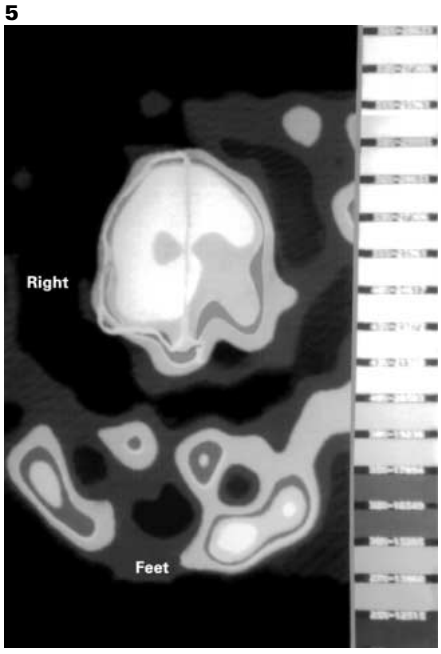




**Fig. 3.** Coronal brain SPECT image showing hypoperfusion corresponding to the left MCA territory in the early period in group 1.
**Fig. 4.** Coronal brain SPECT image showing hypoperfusion corresponding to the left MCA territory in the early period in group 2.



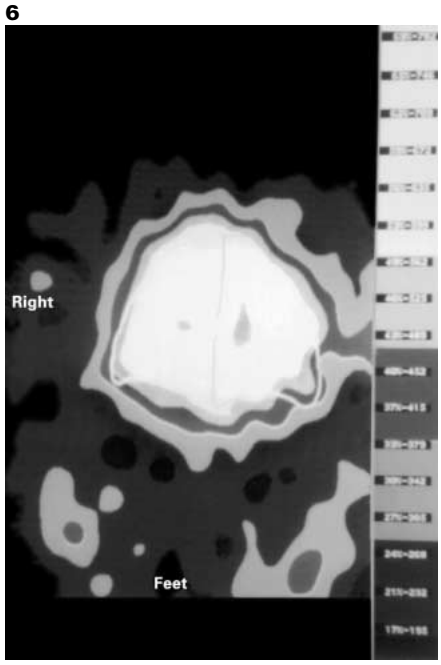




**Fig. 5.** Coronal brain SPECT image showing hypoperfusion corresponding to the left MCA territory in the late period of group 1.
**Fig. 6.** Coronal brain SPECT image showing hypoperfusion limited to a small area of the left inferior parietal lobe in the late period of group 2.

*Statistical Data Analysis*

Paired t test or Wilcoxon signed rank test were used to compare differences within the groups. The Mann-Whitney U test was used for evaluating the degrees of hypoperfusion in SPECT and the volume in MRI imaging in the early and late periods and the values of the neurologic grading scale in the early and late period between the groups. Data are presented as mean ± SD. $p < 0.05$ was considered significant.

## Results

The blood pressures, peripheral oxygen saturation, electrocardiogram and $ETCO_2$ of the animals were similar between the groups and within normal range during the operations, as shown in table 1 ($p > 0.05$).

Mean neurological scores (NS) of both groups are presented in table 2. NS scores in groups 1 and 2 changed

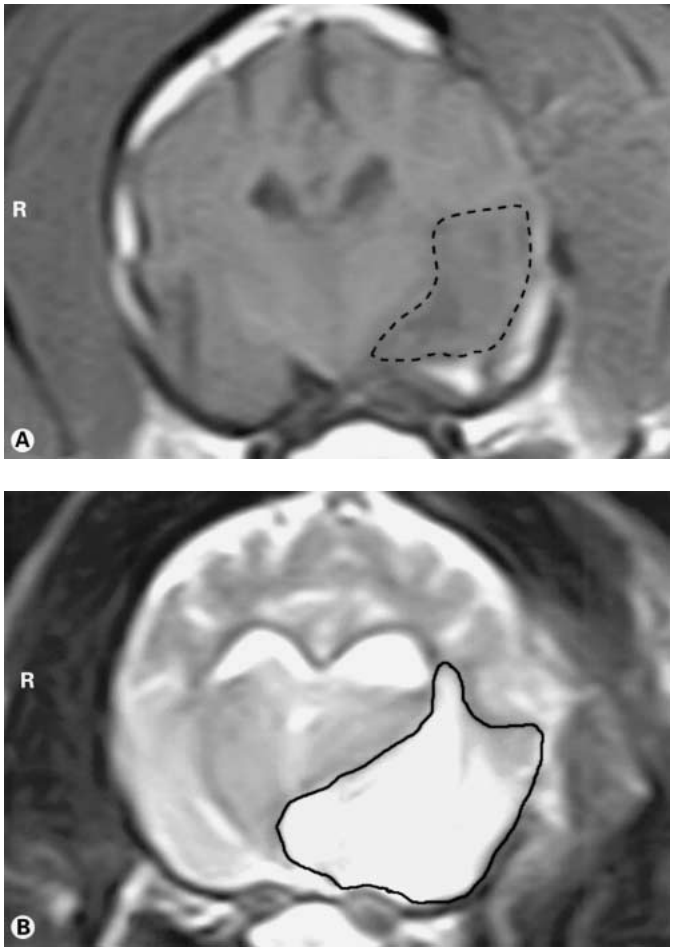



**Fig. 7. A** Coronal T1 W MR image. Hypointensity is seen in the MCA territory in the late period in group 1. The margins of the hypointense lesion are drawn. **B** Coronal T2 W MR image. Hyperintensity is seen in the MCA territory from the cortical area extending to the basal ganglia in the late period in group 1. The margins of the hyperintense lesion are drawn.

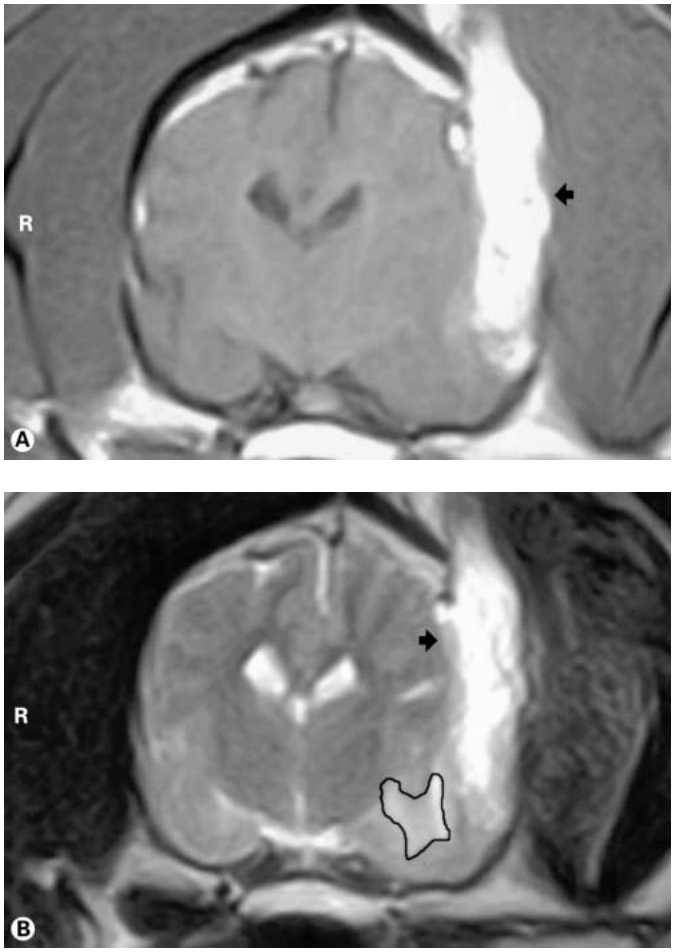



**Fig. 8. A** Coronal T1 W MR image. The isohypointense area can be seen in the left inferior parietal lobe in the late period in group 2, but as it could not be differentiated as a lesion, the margins are not drawn. The arrow shows the transposed omentum. **B** Coronal T2 W MR image. Hyperintensity is limited to a small cortical area of the left inferior parietal lobe in the late period in group 2. The arrow shows the transposed omentum. The margins of the hyperintense lesion are drawn.

significantly between early and late periods ($p < 0.05$). In the early period, there was no difference in NS between the groups ($p > 0.05$), while in the late period, NS of group 2 were higher than NS of group 1 ($p < 0.05$).

Mean hypoperfusion degrees on SPECT imaging of both groups are presented in table 2. Hypoperfusion degrees of groups 1 and 2 were significantly different between early and late periods ($p < 0.001$). In the early period, hypoperfusion corresponding to the left MCA territory on SPECT imaging was similar between the groups ($p > 0.05$; fig. 3, 4). In the late period, the degree of the hypoperfusion in group 2 decreased significantly more than in group 1 ($p < 0.05$; fig. 5, 6).

In the late period, the mean volume of the hypointense lesion in T1 W images was 1,025 ± 122 $mm^3$ and the hyperintense lesion in T2 W images was 2,035.5 ± 287.4 $mm^3$, which was in accordance with ischemic lesion in group 1 (fig. 7A, B). In T1 W images an isohypointense area could be seen in group 2, but it could not be differentiated as a lesion; however, the volume of hyperintense lesion was significantly small in size in group 2 (416.8 ± 62.3 $mm^3$) in T2 W images when compared with group 1 ($p < 0.001$; fig. 8A, B).

## Discussion

Beside intra-abdominal ischemic tissues, a great interest was focused on neovascularization of ischemic cerebral tissue with omentum [4, 7, 11, 20]. Animal experiments have demonstrated that when omental vascularization occurs before MCA occlusion, it could replace the diminished blood flow and protect the brain [5–9]. But omental placement on the brain simultaneous with MCA occlusion or after MCA occlusion had been shown to be ineffective in protecting the animal from cerebral infarction and severe hemiparesis [8]. It was subsequently derived from previous studies that blood vessels developed between the omentum and the underlying brain within 72 h after surgery [21]. Therefore, when omental transposition is performed simultaneously with MCA occlusion, infarction occurs before omental revascularization. So, we thought this model was inappropriate to show the beneficial effect of omental transposition seen in clinical studies [12–16]. Therefore, we proposed a new ischemic model where cerebral ischemic deficit is milder than the deficit produced by MCA occlusion because, in the case of MCA occlusion, blood flow is only provided with cortical anastomosis. But when the ICA and ACB are occluded, contralateral ICA provides the blood flow via RCA and also with cortical anastomosis. Therefore, MCA occlusion produces a more severe ischemia when compared with ICA and ACB occlusion or vice versa. In previous studies, the patients with sufficient collateral blood supply (due to ICA occlusion or severe stenosis of the ICA or large-caliber vessels), no severe completed neurological deficits, and no evidence of any large infarcted area on computerized tomography have shown clinical improvement [12, 13].

In this new ischemic model which resembles the clinical situations not causing cerebral infarction due to sufficient collateral blood supply, beneficial effects of revascularization produced by omental transposition were seen. The animal use committee of our faculty did not allow us to sacrifice the dogs for histological examination. Therefore, we could not obtain histological sections, but we obtained serial T1 W and T2 W MRI images that can define the lesion produced in this ischemia model. In this model, none of the dogs were at grades 1 and 2. All had moderate deficits (grades 3 and 4) during the first 24 h. In the late period, although a significant improvement in NS was observed in both groups when compared with the early period, the improvement in group 2 was more significant than in group 1. In the early period, hypoperfusion over 60% was not observed in any dog in SPECT images. SPECT images were in consistency with the NS of dogs in both early and late periods.

Twenty-four hours after the onset of a stroke, the ischemic or infarcted tissue becomes easily visible on MRI examination [22–25]. Therefore, we did not perform MRI examinations in the first 24 h. However, brain SPECT can show the ischemic tissue after the onset of a stroke; so, only SPECT imaging was performed during the first 24 h. Late SPECT and MRI imaging were performed 72–96 h after the operative procedure because blood vessels developed between the omentum and the underlying brain within 72 h after surgery [21]. So, the effect of omental revascularization could be seen after 72 h.

In conclusion, the benefit of the omental revascularization (by simultaneous transposition of the omentum immediately after the ischemia) was shown clinically and radiologically with brain SPECT examination in a new animal model of cerebral ischemia.

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