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Clinical Article

# Significance of Dynamic MRI in Brain Tumors

Dong-Woo Kim, M.D.[1]
Soon-Ki Sung, M.D.[1]
Young-Jin Song, M.D.[1]
Soon-Seop Choi, M.D.[2]
Dae-Cheol Kim, M.D.[3]
Young-Min Choi, M.D.[4]
Won-Ju Huh, M.D.[4]
Ki-Uk Kim, M.D.[1]

*Departments of Neurosurgery[1] Diagnostic Radiology[2] Pathology,[3] Radiation Oncology[4] College of Medicine, Dong-A University, Busan, Korea*

**Objective :** On the magnetic resonance image (MRI) of the infiltrating brain tumor, enhancement is usually higher in malignant tumor than in benign tumor, and tumor cells can invade into the peritumoral area without definite enhancement. In various pathological conditions, the blood brain barrier (BBB) becomes changed to pathological condition, allowing various materials extravasating into the interstitial space, and degree of enhancement is depend on the pathology. Authors performed dynamic MRI on enhancing and surrounding edematous area in order to evaluate the degrees of opening of BBB, to differentiate tumor from non-tumorous condition, and to determine its relationship with the recurrence of the tumor.

**Methods :** Dynamic MRI was performed in 25 patients. Dynamic scans were done every 15 seconds after administration of Gd-DTPA on the enhancing and surrounding area for maximum 300 seconds, and the patterns of enhancement were analysed. The enhancement curve with initial steep increase followed by slow decrease was defined as "N pattern", those with initial steep increase followed by additional slow increase as "T pattern", and those with initial steep increase followed by plateau as "E pattern". Histopathological findings were compared with the dynamic scan.

**Results :** The graphs taken from enhancing area showed "T pattern" regardless of pathology. In the surrounding area, "T pattern" was noticed in the malignant tumors, but "E pattern" or "N pattern" was noted in low-grade or benign tumors and non-tumorous condition. "T pattern" in the surrounding area was related to the malignancy with tumor cell infiltration and recurrence.

**Conclusion :** The results suggest that the malignant tumor infiltration changes the condition of BBB enough to extravasate the Gd-DTPA. Enhancement pattern in the surrounding edematous area may be a useful information to differentiate the malignant glioma with the low-grade and benign tumors or other non-tumorous conditions.

**KEY WORDS :** Dynamic MRI · Brain tumor · Glioblastoma.

## INTRODUCTION

Even though magnetic resonance image (MRI) is the most useful tool in the diagnosis of brain tumors, it is sometimes difficult to differentiate malignant from benign tumors, tumors from non-tumorous lesions, and tumor recurrence from radiation necrosis. Several methods have been developed for more precise diagnosis that include positron emission tomography (PET), MR spectroscopy, perfusion-weighted MR imaging, and diffusion image. Any one of these methods are not confirmative but combination of these may offer more reliable informations with each method having its own characteristics.

Most of these studies focused on the enhancing areas. Studies focusing on the peritumoral area are limited, even though detailed informations on these area may be very useful in the diagnosis and planning the treatment. Contrast materials will exist in these area if BBB is opened enough to allow the contrast materials pass through. Dynamic scan utilizes the small amount of contrast materials in the peritumoral area, even though it is not enough to induce definite enhancement on the routine MRI.

The study is designed to perform dynamic MRI on the enhancing and surrounding areas to differentiate tumor from non-tumorous condition, high-grade from low-grade tumors, and to determine its relationship with the recurrence of the tumor.

## MATERIALS AND METHODS

A total of 25 patients were included in this study. Seven patients had high-grade gliomas (4 glioblastoma multiformes, 2 anaplastic astrocytomas, 1 anaplastic oligodendroglioma), 1 medulloblastoma. Six patients had low-grade tumors (3 low-grade astrocytomas, 2 gangli-

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• Address for reprints :
Ki-Uk Kim, M.D.
Department of Neurosurgery
College of Medicine, Dong-A University
1 Dongdaesin-dong 3-ga, Seo-gu
Busan 602-715, Korea
Tel : +82-51-240-5241
Fax : +82-51-242-6714
E-mail : kukim@donga.ac.kr

ogliomas, and 1 ependymoma). Other types of pathologies were 5 meningiomas, 2 metastatic brain tumors, 1 primary central nervous system lymphoma, 1 radiation necrosis, and 2 brain abscesses (Table 1). Patient with radiation necrosis did not harbor brain tumor. A 67-year-old male patient with nasopharyngeal carcinoma was treated with irradiation of 7560 cGy, and temporal lobe was included in the radiation field. Brain MRI was taken 36 months after irradiation that showed heterogenously enhancing mass in the temporal area with surrounding edema, and cerebral metastasis or malignant primary brain tumor was suspected before pathological diagnosis. Additional 2 patients had brain abscesses.

Region of interest (ROI) was drawn in the highly enhancing area (EA) and surrounding non-enhancing edematous area (SA) delineating the peritumoral area, and in the normal brain for control study. Ten milliliters of gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) was injected intravenously, and dynamic scan was done every 15 seconds for maximum of 300 seconds. Graphs were made of the data obtained from the dynamic scan, and pattern of enhancement was analyzed. In the normal brain, the enhancement curve showed initial steep increase followed by slow decrease that was defined as "N pattern". It is shown as white curve in Fig. 1D. The graph taken from EA showing initial steep increase followed by additional slow increase similar to logarithmic curve was defined as "T pattern" (yellow curve in Fig. 1D). The enhancement curve with initial steep increase followed by plateau was defined as "E pattern". It is shown as white and red curves in Fig. 2D.

Pre-operative dynamic MRI was taken in 18 patients. Osteoplastic craniotomy for the tumor removal was done and surgical specimen was obtained for the histopathological diagnosis. Postoperative dynamic MRI was taken in 11 patients, 7 patients of these were malignant gliomas, 2 low-grade gliomas,

**Table 1.** Summary of patients characteristic

| Patient No. | Age/ Sex | Diagnosis | Pre-operative | | Post-operative | | Reoperation | F/U (months) |
|---|---|---|---|---|---|---|---|---|
| | | | EA | SA | EA | SA | | |
| 1 | 49/F | glioblastoma multiforme | T | T | T | T | | 36 |
| 2 | 53/F | glioblastoma multiforme | T | T | T | T | | 36 |
| 3 | 60/F | glioblastoma multiforme | T | T | T | T | | 29 |
| 4 | 44/F | glioblastoma multiforme | | | T | T | + | 71 |
| 5 | 57/M | anaplastic astrocytoma | | | | N | | 75 |
| 6 | 51/M | anaplastic astrocytoma | | | T | T | + | 51 |
| 7 | 6/M | anaplastic oligodendroglioma | T | T | T | T | + | 12 |
| 8 | 19/F | medulloblastoma | | | E | N | | 66 |
| 9 | 38/M | astrocytoma, pilocytic | | | | E | | 68 |
| 10 | 1/M | astrocytoma, pilocytic | | | T | N | | 66 |
| 11 | 12/F | astrocytoma, pilocytic | T | N | | | | 41 |
| 12 | 22/F | ganglioglioma | T | E | | | | 63 |
| 13 | 12/F | ganglioglioma | | | T | T | + | 60 |
| 14 | 3/M | ependymoma | T | N | | | | 56 |
| 15 | 49/M | metastatic tumor | T | N | | | | 1 |
| 16 | 53/F | metastatic tumor | T | N | | | | 17 |
| 17 | 28/F | meningioma | T | E | | | | 58 |
| 18 | 69/F | meningioma | T | N | | | | 23 |
| 19 | 62/F | meningioma | T | N | | | | 21 |
| 20 | 44/M | meningioma | T | N | | | | 36 |
| 21 | 59/M | meningioma | T | N | | | | 11 |
| 22 | 55/M | lymphoma | T | E | | | | 3 |
| 23 | 67/M | radiation necrosis | T | E | | | | 1 |
| 24 | 63/M | abscess | T | E | | | | 8 |
| 25 | 58/M | abscess | T | E | | | | 17 |

EA : Enhancing area, SA : Surrounding area, T : "T pattern", N : "N pattern", E : "E pattern", F/U : Follow up

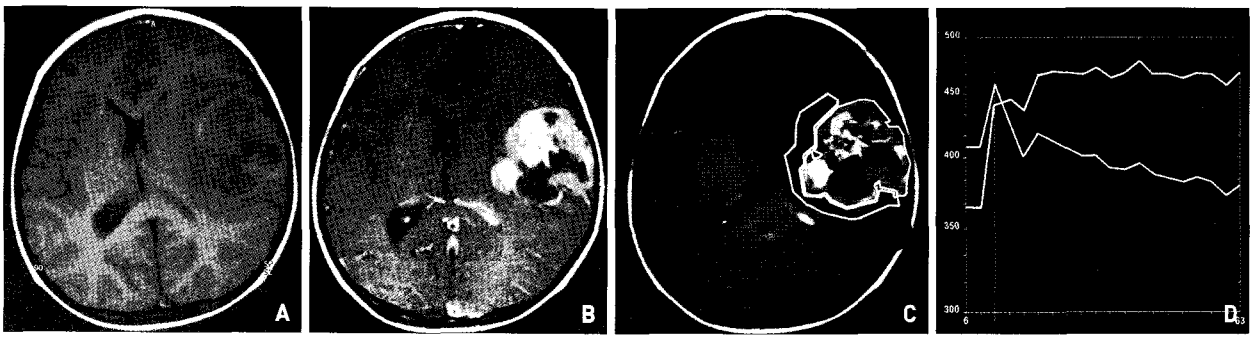


**Fig. 1.** Magnetic resonance images of the brain and dynamic scans were taken on the enhancing and surrounding areas in 3-year-old male patient with intraparenchymal ependymoma (case 14). A : T1-weighted axial image. B : Enhancement with Gd-DTPA. C : Region of interest on the enhancing (yellow) and surrounding (white) areas. D : Dynamic scan on the enhancing area shows "T pattern" (yellow curve) and that on the surrounding area shows "N pattern" (white curve).

1 medulloblastoma, and 1 ganglioglioma. Reoperation was performed in 4 patients with radiological or clinical evidence of tumor recurrence (3 malignant gliomas and 1 ganglioglioma). Dynamic MRI of these patients showed "T pattern" in both EA and SA. The specimens were obtained from the peritumoral edematous area in addition to the enhancing tumor mass.

## RESULTS

In the preoperative study, the graphs taken from EA showed "T pattern" regardless of pathology, but those taken from SA differ according to the pathology. In 4 malignant gliomas, "T pattern" was noted in all cases, but "N pattern" was noted

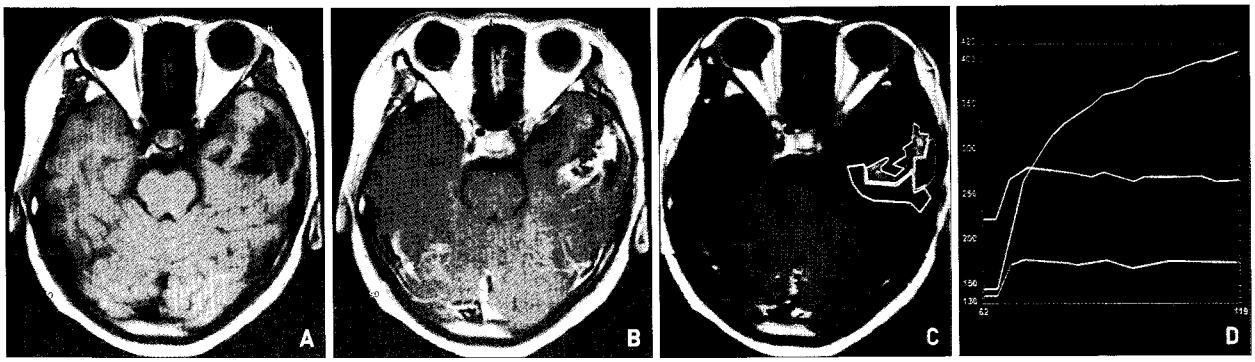


**Fig. 2.** Magnetic resonance images of the brain and dynamic scan were taken on the enhancing and surrounding areas in 22-year-old female patient with ganglioglioma in the left temporal lobe (case 12). A : T1-weighted axial image. B : Enhancement with Gd-DTPA. C : Region of interest for enhancing (yellow) and 2 surrounding (white and red) areas. D : Dynamic scan on the enhancing area shows "T pattern" (yellow) and those on the surrounding areas show "E pattern" (white and red).

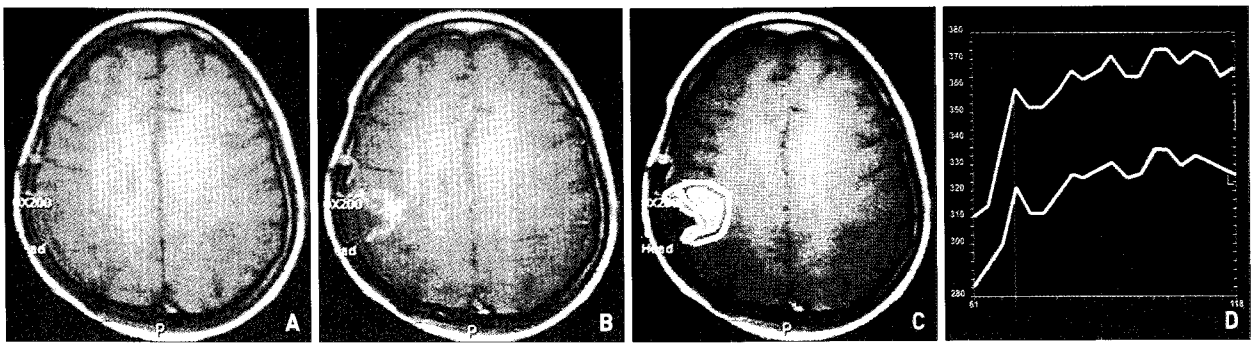


**Fig. 3.** A 44-year-old female patient with glioblastoma multiforme in the right temporoparietal area (case 4). Tumor removal was done followed by irradiation with 59.4 Gy. Magnetic resonance images of the brain and dynamic scan were taken 4 months later. A : T1-weighted axial image. B : Enhancement is noted after administration of Gd-DTPA. C : Region of interest for enhancing (yellow) and surrounding (white) areas. D : "T pattern" is noted in both areas on dynamic scan.

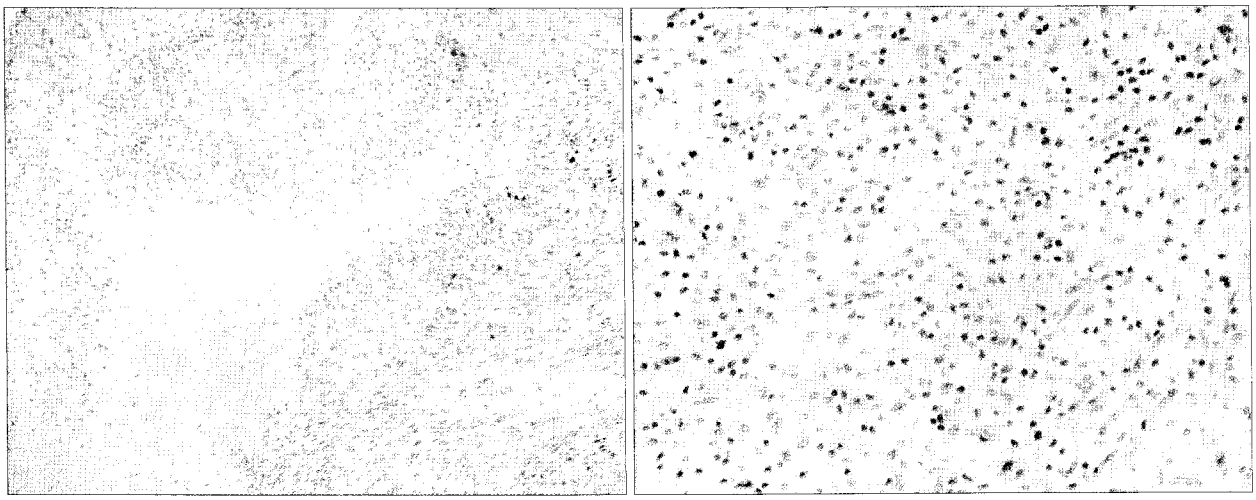

**Fig. 4.** Histopathological findings of the patient with glioblastoma multiforme (case 4). A : The tissue taken from the enhancing area shows hypercellularity, nuclear atypia, mitoses and endothelial proliferation (H&E ×100). B : The tissue taken from the surrounding area is similar to that of the enhancing area (H&E ×200).

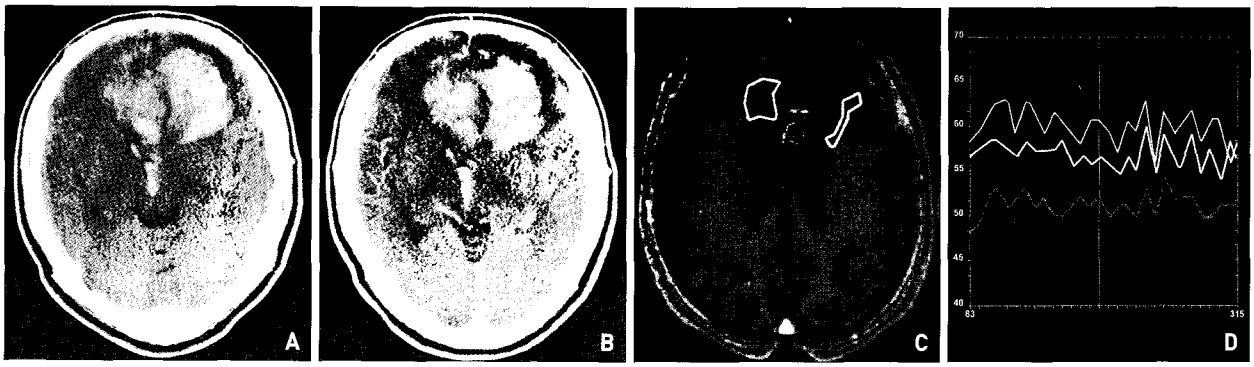


**Fig. 5.** A 57-year-old male patient with anaplastic astrocytoma with tumor bleeding (case 5). A : Pre-contrast image of computed tomography of the brain. B : After administration of contrast materials. C : Magnetic resonance images were taken 4 months after the operation, and dynamic scan was taken from the surrounding areas (yellow, red and white). D : "N pattern" is noted in all areas.

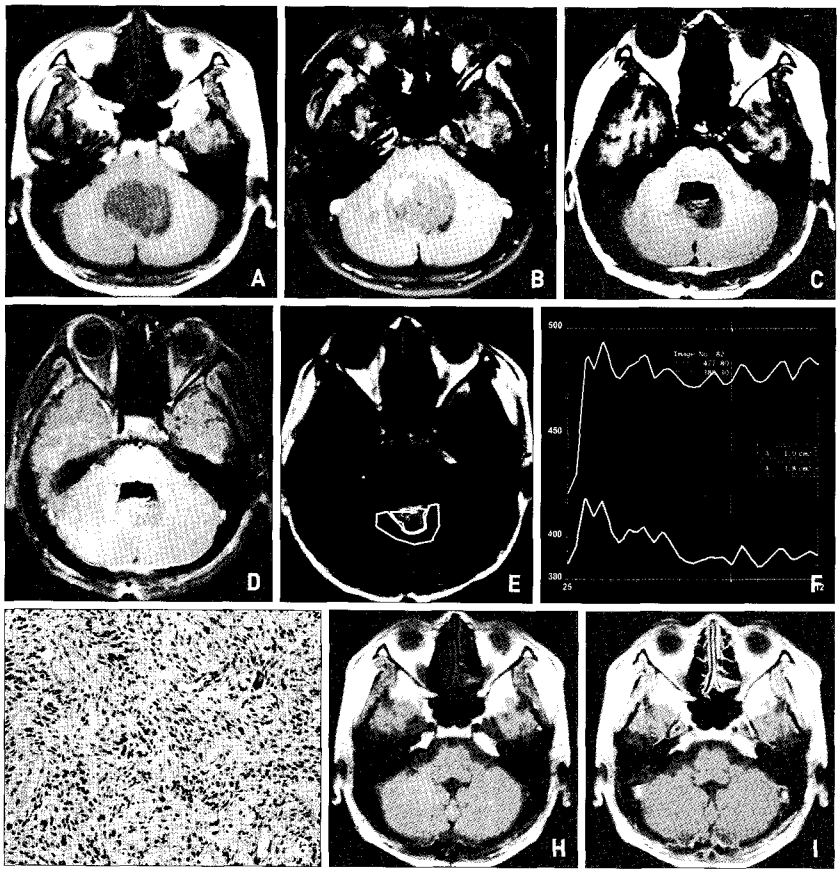


**Fig. 6.** A 19-year-old female patient with medulloblastoma (case 8). A : T1-weighted image of the magnetic resonance image shows low-signal intensity in the posterior fossa. B : Focal enhancement is noted after administration of Gd-DTPA. C : Remnant tumor is noted on the magnetic resonance image taken at the first postoperative day. D : Enhancement is not definite after administration of Gd-DTPA. E : Region of interest on the tumor remnant (yellow) and surrounding (white) areas. F : Tumor remnant area shows "E pattern" (yellow curve) and surrounding area shows "N pattern" (white curve). G : In the pathological finding, tissue shows dysplastic neurons with glial component (H&E ×200). H : T1-weighted image of magnetic resonance image taken 6 months later. I : Enhancement is not noted after administration of Gd-DTPA.

in a low-grade astrocytoma, ependymoma, 2 metastases, and 4 meningiomas (Fig. 1), and "E pattern" was noted in a ganglioglioma, meningioma, lymphoma, radiation necrosis, and 2 brain abscesses (Fig. 2).

The postoperative dynamic MRI was taken in 11 patients. Among 7 malignant gliomas, "T pattern" was noted in both EA and SA in the 6 patients, and reoperation was done in the 3 patients (Fig. 3). After the removal of the enhancing lesion, biopsy was obtained from the peritumoral area and tumor cells were proved to be present in the peritumoral area pathologically (Fig. 4). In an anaplastic astrocytoma (case 5), initial presentation was intracerebral hemorrhage due to the tumor bleeding, and emergency operation was done. After removal of hematoma, tumor tissue was obtained and it was confirmed as anaplastic astrocytoma. Postoperative irradiation of 59.4 Gy was given, and MRI with dynamic scan was taken 4 months later. Abnormal enhancement was not noticed, and dynamic scan on the 3 surrounding areas showed as "N pattern" (Fig. 5).

In patient with medulloblastoma (case 8), preoperative MRI showed decreased signal intensity on T1-weighted image with slight enhancement, unusual finding of the medulloblastoma. MRI taken on the first postoperative day revealed remnant tumor, and dynamic scan revealed "E pattern" in EA and "N pattern" in SA. Radiation therapy consisting of 59.4 Gy was given and tumor recurrence was not noted on the MRI at 6 months (Fig. 6).

In two pilocytic astrocytomas, MRI was taken on the first postoperative day. In case 9, no enhancing lesion was noted, and dynamic scan in SA showed "E pattern". The other patient (case 10) showed small remnant tumor, and dynamic

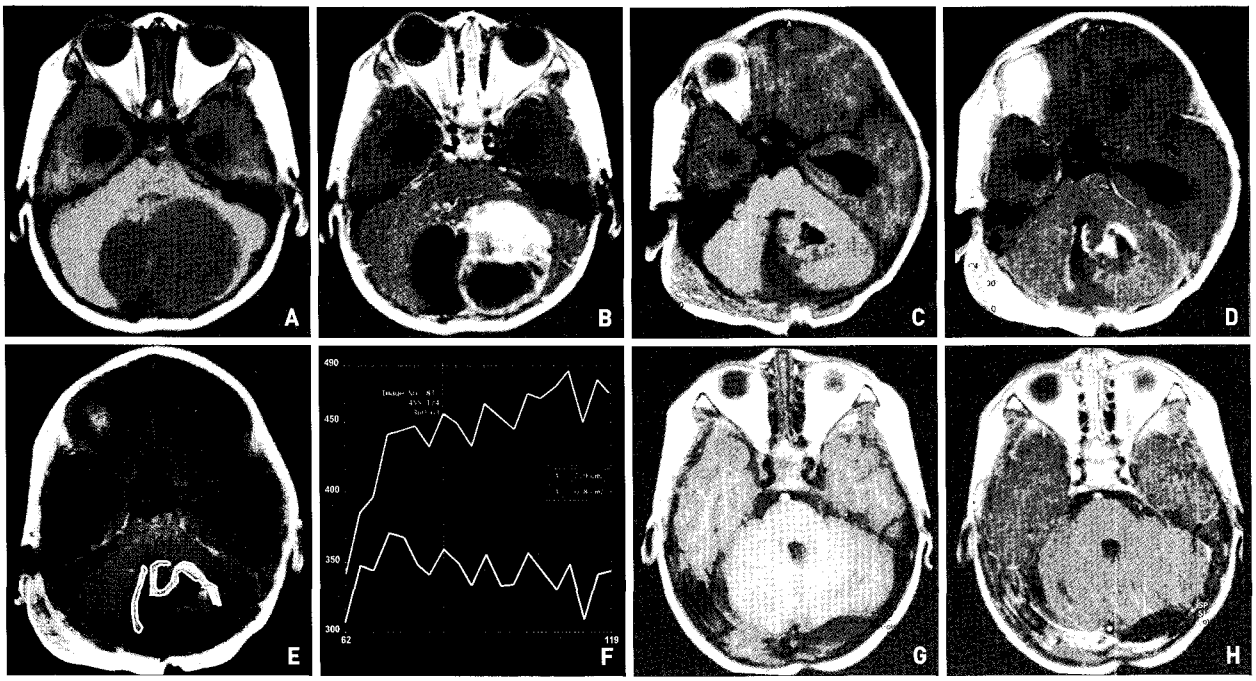


**Fig. 7.** A 1-year-old male patient with pilocytic astrocytoma (case 10). A : T1-weighted image shows low-signal intensity in the posterior fossa. B : Heterogenous enhancement and cystic changes are noted after administration of Gd-DTPA. C : T1-weighted image of the magnetic resonance image taken on the first postoperative day. D : After administration of Gd-DTPA, enhancement is noted along the periphery of the tumor. E : Region of interest on the tumor remnant (yellow) and surrounding (white) areas. F : "T pattern" is noted in the tumor remnant area (yellow curve) and "N pattern" is noted in the surrounding area (white curve). G : T1-weighted image of magnetic resonance image taken 2 year later. H : No evidence of enhancement is noted after administration of Gd-DTPA.

scan showed "T pattern" in the remained enhancing tumor, but "N pattern" was noted in SA (Fig. 7).

In a patient with ganglioglioma (case 13), MRI was taken on the first postoperative day, leaving small area of enhancement at the anterior margin. Dynamic scan showed "T pattern" in both EA and SA. Four years later, tumor recurrence was noted, and reoperation was done (Fig. 8). Histopathologically, the tumor was shown to have glioblastomatous change (Fig. 9). On the contrary, the other patient with ganglioglioma (case 12) who showed "E pattern" in SA by preoperative dynamic scan showed no recurrence up to 63 months.

## DISCUSSION

Many brain tumors show enhancement on MRI after injection of contrast materials because of disruption of BBB. In gliomas, enhancement is related to the pathological grade, the higher is the tumor grade, the stronger is the enhancement. Meningiomas are benign tumors, but show strong enhancement with marked peritumoral edema like glioblastoma. Radiation necrosis may mimic tumor recurrence radiologically and clinically.

Gases and lipid-soluble, small molecular weight molecules, less than 500 dalton, pass across the capillary endothelium in normal condition by diffusion. But, Gd-DTPA, with molecular weight of 547 dalton, can not across it. Extravasation of Gd-DTPA may occur through the neovasculature as well as the disrupted pre-existing vessels.

In normal condition, intravenously injected contrast material pass through the cerebral vasculature, washed out with the blood stream, and no contrast materials are left in the extravascular space. This results in peak concentration of the contrast materials just after injection followed by rapid diminution. In this study, this phenomenen is observed as "N pattern". If contrast materials are extravasated, it will be accumulated in the extracellular space for a while without washing out by the blood stream. After passing through the cerebral circulation, contrast materials go into the systemic circulation and most of the contrast materials will be eliminated. But, still a portion of contrast materials will be remained, and re-enter into the cerebral circulation. During the repeated cerebral circulation, more contrast materials are extravasated, which will increased the concentration of contrast materials in the brain. In this study, this phenomenon was denoted as "T pattern". If BBB is disrupted moderately, allowing limited amount of contrast materials to pass through, the concentration of the contrast materials in the extracellular space will be small, and do not increase significantly after the repeated circulations, causing "E pattern".

The amount of contrast materials should reach to a certain

level in order to exhibit enhancement on MRI. Dynamic MRI can detect smaller amount of contrast materials than routine MRI, and demonstrate it according to its concentration, making concentration graph according to the time sequence.

It is sometimes difficult to differentiate the tumor recurrence or remnant tumor with other conditions showing enhancement such as radiation necrosis. Several methods, such as PET, MR spectroscopy, diffusion imaging of the MRI, have been developed in order to clarify this, but none of these methods are perfect. PET can be utilized as a clinically useful tool for detecting the tumor and its recurrence, estimating its biological aggressiveness, guiding the biopsy, evaluating

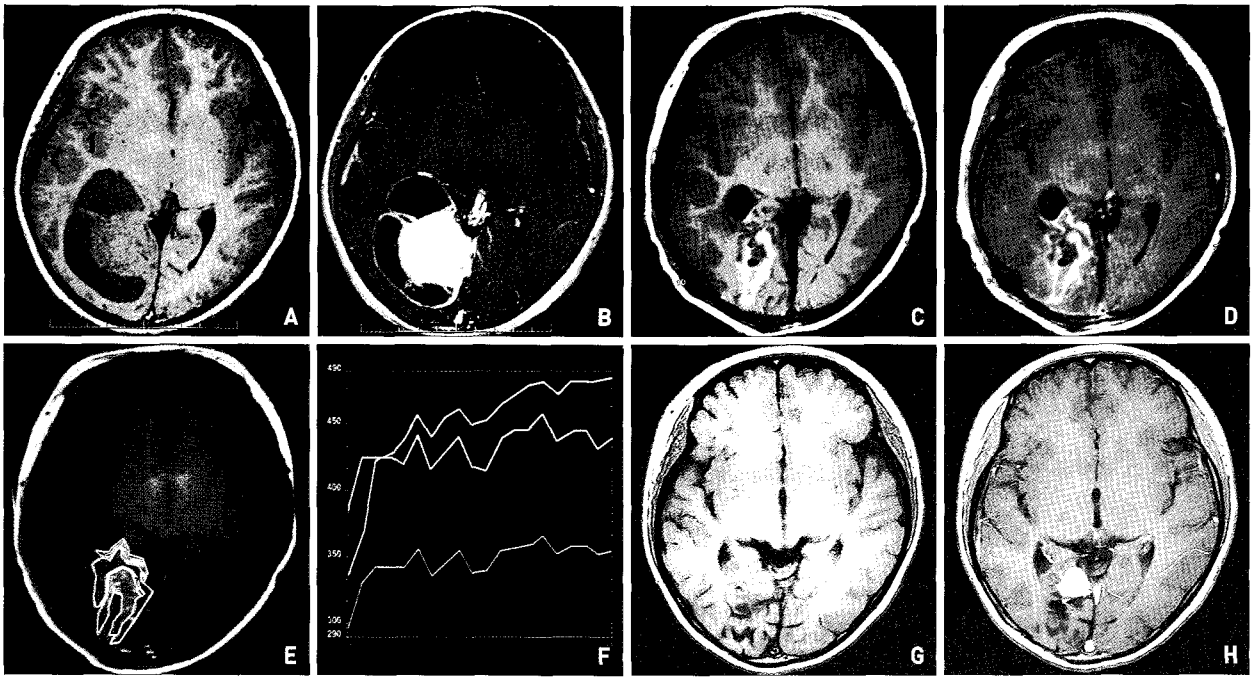


**Fig. 8.** A 12-year-old female patient with ganglioglioma in the right occipital lobe (case 13). A : T1-weighted image shows iso-signal intensity with cyst formation. B : Enhancement is noted after administration of Gd-DTPA. C : T1-weighted image of magnetic resonance image on the first postoperative day. D : Marginal enhancement is noted after administration of Gd-DTPA. E : Region of interest for the enhancing (yellow) and surrounding (white and red) areas. F : "T pattern" is noted in all areas. G : T1-weighted image of the magnetic resonance image taken 4 years later. H : Strong homogenous enhancement is noted after administration of Gd-DTPA.

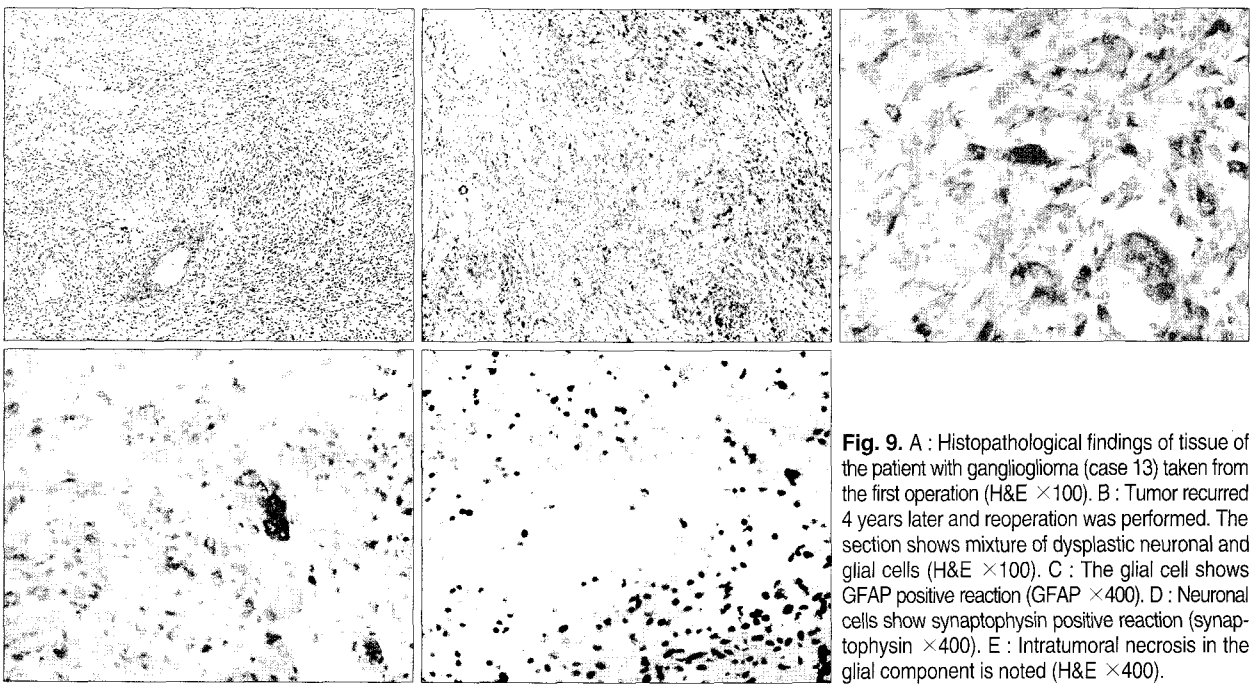

**Fig. 9.** A : Histopathological findings of tissue of the patient with ganglioglioma (case 13) taken from the first operation (H&E ×100). B : Tumor recurred 4 years later and reoperation was performed. The section shows mixture of dysplastic neuronal and glial cells (H&E ×100). C : The glial cell shows GFAP positive reaction (GFAP ×400). D : Neuronal cells show synaptophysin positive reaction (synaptophysin ×400). E : Intratumoral necrosis in the glial component is noted (H&E ×400).

the response to the therapy, and delineating the target volume in radiation therapy[1]. The glucose metabolic rate is increased in gliomas, and is related to the pathological grade. It seems to be a good predictor of their biological behavior and aggressiveness. Fluorodeoxyglucose (FDG) utilize the glucose channel, and is used as a tracer of PET, and it was reported to have correlation with histological grading and patients survival[9,10]. In addition to FDG, biomarkers that can be used in PET imaging include Fluorine-18 fluorothymidine (F-18 FLT), [(11)C]hemicholinium-15 and- [(18)F] hemicholinium-15, [(18)F]-choline, [(18)F]-fluoromisonidazole (Fmiso), and [(11)C]-methionine (MET)[5,13]. Prospective study was performed to differentiated recurrent cerebral astrocytoma from radiation necrosis using (13)N-NH(3) PET, and (13)N-NH(3) was suggested as a promising tracer for this purpose, because (13)N-NH(3) uptake was increased in the recurrent astrocytomas compared to absent or less (13)N-NH(3) uptake in the radiation necrosis[14]. In a study to evaluate the relationship between tumor vascularity and amino-acid metabolism, the maximum regional cerebral blood volume ratio and maximum MET uptake ratio were reported to correlate significantly in gliomas[12]. Because the above radioligands work through the different pathways, the PET informations, obtained using each tracer, can be different, and prognostic accuracy will be increased by combination of these methods. Even though PET is a useful diagnostic tool for the lesions with abnormal enhancement, it does not provide any information to the peritumoral area in which enhancement is not noted.

Spectroscopic data can be obtained by the resonant frequency of a spin determined by the molecules, such as myoinositol, choline, creatine, phosphocreatine, glutamate, glutamine, N-acetyl aspartate (NAA), and lactate. Among many situations causing abnormal enhancement on MRI, changes of the molecules by metabolic end-result will be different. Increased choline resonance can be seen in proliferating tumors, and MR spectroscopy may be used as a tool in differentiating the tumors and other conditions causing enhancement[11]. MR spectroscopy may be useful in differentiating tumor recurrence and radiation necrosis by observing the choline/creatine ratio and lactate peak, and in differentiating high-grade and low-grade gliomas through choline/creatine and lactate/creatine ratios[7]. When tumor tissue is exposed to irradiation, metabolic changes will occur. After gamma knife radiosurgery for metastatic brain tumors, significant reduction of choline/creatine and NAA/creatine ratios are reported to occur on the proton MRS of the tumor[3]. In gliomas, tumor cells are present in peritumoral non-enhancing area in addition to the enhanceing mass. Also, tumor recurrence after initial treatment will occur from the periphery of the tumor. Metabolic status in the peritumoral area has been studied with long-echo proton MR spectroscopy, by which significant decrease of NAA and more frequent presence of lactate are found. Lactate in the peritumoral area was thought to be originated from the tumor cells and spread into the peritumoral area by diffusion[4].

Neovascular formation occurs in brain tumors and changes in microvasculature may differ according to the types of tumors. It is expected that rapidly growing tumors have more vascularity than relatively slow-growing tumors. Perfusion-weighted MR imaging was investigated for various lesions, and many parameters, such as relative cerebral blood volume, absolute cerebral blood flow, cerebral blood volume, mean transit time, and fractional plasma volume, were measured. Of these, relative cerebral blood volume was suggested to be the best parameter not only in differentiating certain kinds of tumor with the other but also in glioma grading[6,8]. Data of the perfusion MRI after irradiation may be useful in the differential diagnosis between tumor recurrence and radiation necrosis. Gradient and spin-echo T2-weighted, gadolinium-enhanced T1-weighted and DSCE perfusion MR imaging were obtained from regions of interest with known radiation injury. The mean transit time was prolonged in both the High Dose Zone and the Intermediary Dose Zone. The relative cerebral blood volume and relative cerebral blood flow index were decreased in the High Dose Zone but not in the Intermediary Dose Zone[2]. Perfusion MR imaging may not be expected to give definite information to the area of recent tumor formation where neovascular formation do not mature yet, but it is advisable to combine perfusion MR imaging with dynamic study to increase the accuracy of preoperative diagnosis, and to estimate tumor grade and to differentiate tumor recurrence and radiation necrosis.

## CONCLUSION

It is suggested that dynamic MRI on the surrounding non-enhancing edematous area may be a very useful tool in the differential diagnosis between tumors and non-tumorous lesions, high-grade and low-grade tumors, and tumor recurrence and other conditions, such as radiation necrosis. It is recommended to combine the results of dynamic MRI with those of PET, MR spectroscopy, perfusion-weighted imaging, and diffusion images to increase the accuracy of diagnosis.

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