Preoperative depiction of cavernous sinus invasion by pituitary macroadenoma using three-dimensional anisotropy contrast periodically rotated overlapping parallel lines with enhanced reconstruction imaging on a 3-tesla system

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Object. Three-dimensional anisotropy contrast (3DAC) magnetic resonance (MR) imaging provides clear depiction of neuronal fibers. The aim of this study was to identify intracavernous cranial nerves in patients with pituitary macroadenoma and in healthy volunteers by using 3DAC MR imaging on a 3-tesla system and to preoperatively predict cavernous sinus invasion by pituitary macroadenoma.

Methods. Thirty-three patients (cavernous sinuses in 66 sides) with pituitary macroadenomas and 25 healthy volunteers (50 sides) participated in this study. Coronal 3DAC MR images constructed from diffusion weighted images, acquired with periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) sequences, and T2-weighted reverse images were obtained at the same anatomical locations using a 3-tesla MR imaging system.

Attempts were made to identify the cranial nerves.

Results. The oculomotor and ophthalmic/maxillary nerves were preoperatively identified in all sides (66 sides in patients and 50 sides in healthy volunteers) on 3DAC MR images. In the 33 patients, cavernous sinus invasion was revealed in 10 (12 [18.2%] of 66 sides) by intraoperative endoscopic observation. Coronal 3DAC MR images revealed that the oculomotor nerves were half surrounded with adenoma in all 12 of these sides, and the ophthalmic/maxillary nerves were half encapsulated with tumor (sensitivity/specificity: 100%/100% and 83%/100%, respectively).

Conclusions. Preoperative evaluation of pituitary macroadenomas using 3DAC PROPELLER MR imaging on a 3-tesla system is likely to be a powerful noninvasive method of detecting cavernous sinus invasion, which can potentially dominate the therapeutic strategy for these lesions. (DOI: 10.3171/JNS/2008/108/01/0037)

Key Words • cavernous sinus invasion • cranial nerve • pituitary macroadenoma • PROPELLER • three-dimensional anisotropy contrast

Six to 10% of pituitary adenomas involve the cavernous sinus in their extension, 1,6 and are considered invasive. 12,13 Because the intracavernous cranial nerves are lateral to the intracavernous internal carotid artery, 7 clinical signs of cavernous sinus invasion occur late, irrespective of lesion size. Invasion is a feature of biologically aggressive neoplasms and increases the morbidity and mortality rates associated with surgical procedures even though the tumor remains histologically benign in most cases. 11 Today, endoscopic transsphenoidal surgery 2,3,9,10 and stereotactic radiosurgery can be performed for a pituitary adenoma invading the cavernous sinus. 7,8 Both of these advanced therapeutic modalities require more accurate identification of the sinus invasion and localization of the intracavernous cranial nerves involved by the tumor to optimize treatment efficacy and reduce the risk of damage to cranial nerves during the procedures. Although several authors have advocated the use of predictive criteria to identify sinus invasion by pituitary adenoma based on meticulous analyses of MR images, 5,11,21 the preoperative diagnosis of sinus invasion remains a matter of probabilistic inference given that direct intraoperative observation is frequently the only way to distinguish between sinus compression from lesions and actual sinus invasion by tumor. 12

Three-dimensional anisotropy contrast MR imaging, one of the fiber orientation weighted imaging techniques, is widely used in neurological and neurosurgical fields, 8,14,15, 22,23 In particular, the use of 3DAC MR imaging based on PROPELLER sequences 16 on a 3-tesla system provides the synergistic effect of high signal-to-noise ratio and has excellent contrast for anatomical resolution in all areas of the human brain (Fig. 1). 14,19 Therefore, it seems plausible for 3DAC PROPELLER MR imaging to be a reliable and useful method of detecting sinus invasion by pituitary macroadenoma.

The purpose of the present study was as follows: 1) to identify the intracavernous cranial nerves in patients with pituitary macroadenomas and in healthy volunteers by us-

Abbreviations used in this paper: DW = diffusion weighted; MR = magnetic resonance; PROPELLER = periodically rotated overlapping parallel lines with enhanced reconstruction; 3DAC = three-dimensional anisotropy contrast.
ing 3DAC PROPELLER MR sequences on a 3-tesla system; 2) to compare preoperative 3DAC MR images of the cavernous sinus with intraoperative high-resolution endoscopic observations; and 3) to assess the predictive value of preoperative findings of cavernous sinus invasion by the adenoma on 3DAC MR images.

Clinical Material and Methods

Study Population

This study was performed according to the human research guidelines of the internal review board of the University of Niigata. Thirty-three patients (15 male and 18 female) with a mean age of 53.7 years (range 19–74 years) and harboring a pituitary macroadenoma participated in the study. The lesions included 25 nonfunctioning, 4 prolactin-secreting, and 4 growth hormone–secreting adenomas. All participants underwent concurrent neurological and ophthalmological examinations and were evaluated by neuro-ophthalmologists. Twenty-five healthy volunteers (12 male and 13 female) also participated in the study.

Magnetic Resonance Imaging

All patients and control volunteers underwent identical MR imaging evaluations. A General Electric Signa 3.0T system was used to perform all MR imaging. Coronal 3DAC MR images were processed using a previously reported method based on DW images acquired with PROPELLER sequences. The following parameters were used for DW imaging: coronal slices 4, field of view 200 × 200 mm, matrix 256 × 256, slice thickness 5 mm, echo train length 12, interslice gaps 7.5 mm, TR 4000 msec, TE 72.7 msec, and number of excitations 3. The b-value was 770 seconds/mm² for each axis with the 4 combinations of diffusion-gradient vectors as follows: (0, 0, 0), (0, 0, 1), (1, 0, 0), and (0, 1, 0), where the (x, y, z) direction corresponded to right-left, anterior-posterior, and superior-inferior courses in the brain in the supine position. Parameters for the motion-proving gradient were as follows: amplitude 3.6 G/cm, ramp time 600 μsec, Δ 29 msec, and δ 19 msec. The total scanning time for acquisition of the entire DW imaging data set was ~17 minutes.

The T2-weighted reverse images were acquired with a short inversion time inversion recovery sequence by using the following parameters: coronal slices 4, field of view 200 × 200 mm, matrix 512 × 512, slice thickness 5 mm, interslice gaps 7.5 mm, TR 4000 msec, TE 23 msec, inversion time 175 msec, and number of excitations 2. In the acquisition of 4 serial coronal 3DAC MR images, a second slice was acquired at the infundibular stalk and/or a third slice was acquired at the mamillary bodies, which was secured even in cases of a large adenoma. Coronal T2-weighted reverse images were acquired in the same way as the coronal 3DAC MR images.

Intracavernous Cranial Nerves

In this study, the oculomotor, trochlear, ophthalmic/maxillary, and abducent nerves were evaluated as intracavernous cranial nerves. As a matter of practical convenience, we considered the oculomotor nerves as the upper marker of the cavernous sinus indicators and the ophthalmic/maxillary nerves as the lower by using the above-described coronal MR images.

Evaluation of 3DAC MR Axonography Following Intraoperative Observation

Endoscopic endonasal transsphenoidal surgeries were performed by one experienced neurosurgeon. All operations were recorded using a digital video recorder. In all cases, tumor samples were sent to neuropathologists for histological diagnosis. Whether patients had sinus invasion was determined during endoscopic surgeries and confirmed on recorded videotapes. The comparisons between MR imaging results and surgical findings were conducted independently, but the outcome was resolved through consensus. Statistical analysis of the results was performed using the Fisher exact test.

Results

In the 25 healthy volunteers, the oculomotor nerve was identified in 50 (100%) of 50 cavernous sinus sides, the trochlear nerve in 38 (76%), the ophthalmic/maxillary nerves in 50 (100%), and the abducent nerve in 36 (72%) on 3DAC PROPELLER MR images (Fig. 2). In the 33 patients with pituitary macroadenomas, the oculomotor nerve was detected in 66 cavernous sinus sides (100%), the trochlear nerve in 29 (44%), the ophthalmic/maxillary nerves in 66 (100%), and the abducent nerve in 25 (38%) on 3DAC MR images (Figs. 3 and 4). Preoperatively diagnosed pituitary macroadenomas were all confirmed by histopathological reports. Postoperative damage to visual systems and intracavernous sinus cranial nerves

![Fig. 1. Typical axial (A), coronal (B), and sagittal (C) 3DAC PROPELLER MR images demonstrating normal anatomy.](image-url)
was not observed in this series of participants. Based on intraoperative endoscopic observation and postoperative video review, cavernous sinus invasion was confirmed in 12 (18.2%) of 66 sides and in 10 (30%) of 33 patients (Fig. 5). Coronal 3DAC MR images revealed the following: 1) the oculomotor nerve was half surrounded with pituitary adenoma in all 12 cavernous sinuses invaded by tumor; 2) the oculomotor nerve was not surrounded with tumor in the remaining 54 cases of uninvaded cavernous sinuses (Fig. 3); 3) the ophthalmic/maxillary nerves were half surrounded with tumor in 10 of the 12 invaded sinuses; and 4) these nerves were not surrounded with tumor in the remaining 54 cases of uninvaded sinuses. In this study, “half surrounded” was defined as “having contact with the tumor on the upper, lower, and medial surface of the nerve.”

The 3DAC findings of the oculomotor and ophthalmic/maxillary nerves surrounded by pituitary adenoma were significantly (p < 0.001) associated with cavernous sinus invasion by the adenoma (sensitivity/specificity: 100%/100% and 83%/100%, respectively).

The mean follow-up period in the 33 patients was 19.5 months (range 10–27 months). During the follow-up, neither recurrence nor regrowth of the tumor was observed even in the patients with cavernous sinus invasion.

**Discussion**

Three-dimensional anisotropy contrast PROPELLER MR imaging on a 3-tesla system is characterized by extraordinary contrasts for neuronal fibers such as cranial nerves and neural tracts and enables clear depiction of intracavernous cranial nerves even in pituitary adenomas. In the present study, in particular, the oculomotor and ophthalmic/maxillary nerves, regardless of whether there was cavernous sinus invasion, were demonstrated with good reproducibility using 3DAC MR imaging. For clinical use, the oculomotor and ophthalmic/maxillary nerves on the 3DAC
the medial wall of the cavernous sinus is intact, the medial surfaces of the cranial nerves running in the lateral wall of the sinus can make contact but are, we believe, unable to touch both the upper and lower surfaces (Fig. 5B and 7 left). On the other hand, when the medial wall is broken due to invasion by the adenoma, cranial nerves running in the lateral wall can make contact with the tumor on the wide plane (Figs. 4 and 5C). Therefore, considering the location of the cranial nerves running within the lateral wall of the cavernous sinus, without relying on statistical analysis, it seems plausible that the 3DAC MR findings that show tight contact between pituitary macroadenomas and the intracavernous cranial nerves, especially the oculomotor and ophthalmic/maxillary nerves, indicate cavernous sinus invasion. Although the distinction between invasion and compression can be somewhat difficult to determine in some cases, the postoperative MR imaging results were well correlated with the intraoperative endoscopic observations as well as the preoperative MR imaging findings that show tight contact between pituitary macroadenomas and the intracavernous cranial nerves. The oculomotor nerves were totally removed by exposing the intact medial wall of the cavernous sinus, which was observed bilaterally under endoscopic vision; postoperative MR images revealed no residue of the tumors (Figs. 5B and 7). Hence, preoperative evaluation of pituitary macroadenomas using 3DAC PROPELLER MR imaging appears to be a powerful noninvasive method that can potentially dominate therapeutic planning for these lesions.

Although previously described methods of evaluating cavernous sinus invasion by macroadenomas via conventional MR imaging remain clinically useful, they seem to be somewhat unreliable because of the thinness of the medial wall of the cavernous sinuses and the variability in the shape, size, and distribution of the venous plexus in the sinuses. Moreover, because previously reported studies on cavernous sinus invasion are fundamentally based on recursive prediction derived from extent adenoma findings on conventional computed tomography or MR imaging, it is clear that they have limitations regarding the detection of sinus invasion. In the present study, we found a more reliable method of detecting cavernous sinus invasion, that is, identifying the oculomotor nerves and ophthalmic/maxillary nerves half surrounded with pituitary macroadenoma by using 3DAC PROPELLER MR imaging. This method can be used to diagnose invasion of the cavernous sinus by an adenoma and to directly visualize the location of the invasion preoperatively.

In this study, on 3DAC PROPELLER and T2-weighted reverse MR imaging, the ability to detect the trochlear and abducent nerves was lower than that for the oculomotor

![Fig. 5. Intraoperative photographs demonstrating medial walls of the cavernous sinus in cases of noninvasive pituitary macroadenomas (A and B, same cases as in Figs. 3 and 7, respectively) and an invasive macroadenoma (C, same case as Fig. 4). Note the flat and intact medial wall (yellow star, A) of the cavernous sinus, the concave but intact medial wall (yellow star, B and C), and the wall with a defect (yellow triangle, C). Black stars represent the dura mater; yellow circle, the diaphragm of the sella.](image)

![Fig. 6. Schematic overview demonstrating the differences between the right cavernous sinus and normal anatomy (A), a noninvasive pituitary macroadenoma (B), and an invasive pituitary macroadenoma (C). The positional relationship of intracavernous sinus cranial nerves and adenoma depends on whether the medial wall is intact or broken. III = oculomotor nerve; IV = trochlear nerve; V1 = ophthalmic nerve; V2 = maxillary nerve; VI = abducent nerve.](image)
and ophthalmic/maxillary nerves even in the healthy volunteers because these nerves were anatomically very tiny and thin. Moreover, the medial walls of the cavernous sinus could not be observed using our method. Hence, further studies are definitely warranted to confirm the reliability and reproducibility of the present data to improve spatial resolution for the depiction of the trochlear and abducens nerves and the medial wall of the cavernous sinus itself for clinical application.

**Conclusions**

Evaluation of pituitary macroadenomas using 3D AC PROPELLER MR imaging on a 3-tesla system provides a noninvasive means of preoperatively assessing cavernous sinus invasion, which can potentially dominate the therapeutic strategy for these lesions.

**References**


Fig. 7. Preoperative (left) and postoperative (right) 3DAC MR images of the macroadenoma without cavernous sinus invasion. When pituitary macroadenomas protrude in the direction of the cavernous sinus and the preoperative 3DAC MR image shows no cavernous sinus invasion, the adenoma will be totally removed with rare exceptions. Figure 5B features an intraoperative photograph from this case.