



CLINICAL INVESTIGATIVE STUDY

Diffusion-weighted and dynamic contrast-enhanced MRI to assess radiation therapy response for head and neck paragangliomas

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ABSTRACT

Background and Purpose: The prediction of radiotherapy outcome in head and neck paragangliomas is clinically important. We investigated perfusion and diffusion markers for evaluation of response to radiotherapy of head and neck paragangliomas.

Methods: We retrospectively reviewed 330 consecutive patients from January 2016 to September 2019 with suspected head and neck paragangliomas, and enrolled 11 patients (2 males, 9 females; age: 55.2 ± 10.3 years) who had conventional MRI and dynamic contrast-enhanced (DCE)-MRI before and after radiation therapy. Radiation therapy, consisting of external beam radiotherapy or stereotactic radiotherapy, was conducted at the radiation oncology department in a single center. Mean apparent diffusion coefficient (ADC), normalized mean ADC, and parameters of DCE-MRI were compared between pre- and post-treatment status by paired t-test. The Pearson correlation coefficient was used for the relationship between tumor volume ratio (post-treatment status/pre-treatment status) and pre-treatment and post-treatment values.

Results: Mean and normalized ADC values were statistically higher in post-treatment status than pre-treatment status ($p = 0.005$, $p = 0.005$, respectively), and Ktrans (volume transfer constant between extravascular, extracellular space [EES], and blood plasma per minute) and Kep (rate transfer constant between EES and blood plasma per minute) were significantly lower in post-treatment status than pre-treatment status ($p = 0.007$, $p = 0.027$, respectively). The correlation coefficient of the relationship between tumor volume ratio and pre-treatment Ktrans ($r = 0.70$; $p = 0.016$) and between tumor volume ratio and post-treatment Ktrans and Kep ($r = 0.83$; $p = 0.002$, $r = 0.8$; $p = 0.003$, respectively) was statistically significant.

Conclusions: Ktrans has predictive potential to predict the response to radiation therapy of head and neck paragangliomas.

KEYWORDS

DCE-MRI, DWI, head and neck, paraganglioma, radiation therapy

INTRODUCTION

Paragangliomas are uncommon neuroendocrine tumors arising from the sympathetic and parasympathetic autonomic system and occur

anywhere from the base of the skull to the pelvis. Seventy percent of extra-adrenal paragangliomas arise in the head and neck region, with an estimated annual incidence of 3–8 cases per 1 million people in general population.¹ The typical clinical sites of head and neck paragangliomas are the carotid artery bifurcation, the middle ear, and jugular fossa.^{1–3} On conventional MRI, paragangliomas usually show hypointensity on T1-weighted images, isointensity to hyperintensity on T2-weighted images, and intense heterogeneous enhancement on contrast-enhanced T1-weighted images. Signal voids related to the high flow within the tumor are common with a “salt-and-pepper appearance.”⁴ In carotid bifurcation lesions, splaying of the carotid bifurcation has been described on MRI and computed tomography (CT) angiography.⁴ Treatment options for paragangliomas include surgery and radiation therapy (RT), which depends on the location, size of the tumor, patient’s age and condition, or the anticipated morbidity of the treatment alternatives.⁵

Typically, RT is chosen to treat when the patients are elderly, or when the tumor is deemed unresectable. The goal of RT is to halt further tumor progression. Generally, the size of the treated residual mass is stable or gradually regresses, and it is extremely rare for the mass to completely disappear.⁵ As long as the tumor does not progress, treatment goals have been met. In fact, the cumulative rate of local size control is approximately 90%⁶ with rare cases of progression after RT. Radiation-associated imaging changes on MRI include decrease of flow voids within the tumor, decreased heterogeneous enhancement, and reduced T2 signal of tumor.⁷ However, there have not been any established parameters for detection of the response to RT in head and neck paragangliomas. Recently, magnetic resonance techniques, such as diffusion-weighted imaging (DWI)⁸ and dynamic contrast-enhanced (DCE)-MRI,^{9,10} have been proposed as such non-invasive imaging parameters for prediction and early detection of response to cancer therapy for various organs. DWIs can be used for diagnosis, staging, and follow-up of head and neck tumors¹¹ based on the fact that apparent diffusion coefficient (ADC) value can reflect the solid tumor’s cellularity. DCE-MRI demonstrates functional characteristics of the tumor, such as vascularity and permeability. Therefore, DWI and DCE-MRI can allow for evaluation of the RT response.

This study investigated these values for prediction of RT response in head and neck paragangliomas.

METHODS

Our institutional review board approved this retrospective single-center study and waived the requirement for informed consent. Data were acquired in compliance with all applicable Health Insurance Portability and Accountability Act regulations.

Study population

We retrospectively reviewed the medical records of 330 consecutive patients from January 2016 to September 2019 who were suspected

of head and neck paragangliomas. There were 94 patients who were diagnosed with paragangliomas histopathologically, or clinically diagnosed by elevated plasma fractionated metanephrines or elevated 24-h urinary fractionated metanephrines, imaging findings of head and neck conventional CT and MRI, and positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro-D-glucose integrated with CT or ¹¹¹In-pentetreotide single-photon emission CT. We excluded patients who had been previously treated with operation or embolization, or did not have pretreatment or post-treatment DWI and DCE-MRI.

Eleven patients (2 males, 9 females; age 55.2 ± 10.3 years; age range 36–69 years) who had pre- and post-treatment DWI and DCE-MRI were included in this study. Four patients were pathologically proven, and seven patients were clinically diagnosed. Post-treatment conventional MRI and DCE-MRI were performed 12 months after RT. After RT, any direct procedures or interventions, such as biopsies, or any additional treatments, such as surgery, chemotherapy, or embolization, were not performed.

Radiation therapy

All patients had conventional external beam radiation therapy (EBRT) or stereotactic radiotherapy at the radiation oncology department in our institution.

The dose of 45 or 50 gray for 25 fractions of EBRT was delivered to eight patients. The dose of 25 or 30 gray for five fractions of stereotactic radiotherapy was delivered to three patients.

MRI acquisition

MRI examinations were performed using 1.5T and 3T (Ingenuia; Philips, Eindhoven) with a head and neck array coil in supine position. Pre and post T1-weighted images and DWI were used in this study. The parameters of pre- and post T1-weighted images were as follows: plane = axial and coronal, repetition time (TR) = 500–800 ms, echo time (TE) = 5–16 ms, NEX = 1 or 2, slice thickness/gap = 3.5-5/1-1.2 mm, field of view = 180–240 mm, and matrix = 188–320×188–320. DWI used echo-planar imaging. Sensitizing diffusion gradients were applied sequentially with *b* values set at 0 and 1000 s/mm². The parameters of DWI were as follows; plane = axial, TR = 5000–10000 ms, TE = 58–106 ms, NEX = 1 or 2, slice thickness/gap = 3.5-4/0-1 mm, field of view = 220–260 mm, matrix = 128–200 × 128–200, diffusion directions = 3. DCE-MRI sequence was performed using three-dimensional T1-weighted images of 3D-T1 fast field echo (FFE), with the administration of contrast gadobenate dimeglumine (Multi-hance, Bracco diagnostics, Singen, Germany). An intravenous bolus of 20 ml of gadobenate dimeglumine was administered using a power injector with a flow rate of 5.0 ml/s through a peripheral arm vein, followed by a 20 ml saline flush. DCE-MRI was sequentially obtained for 30 dynamic phases for each investigation. These techniques were performed on all image systems in a single center. The parameters of 3D-T1 FFE were as follows: TR = 4.6 ms, TE = 1.86 ms, flip



angle = 30°, slice thickness = 5.0 mm; field of view = 240 × 240 mm², voxel size = 1.0 × 1.0 × 5.0 mm³, NSA = 1, number of slices per dynamic scan = 48 slices, temporal resolution = 8.4 s, and total acquisition time of 4 min and 13 s, using 16-channel NeuroVascular coil.

DATA ANALYSIS

Patients' demographics

The patient's demographics were reviewed from electrical medical records, and included the following information: age, sex, location of the tumor, details of RT, pre-treatment tumor size, and volume ratio of the tumors between pre- and post-treatment.

Imaging analysis

One board certified neuroradiologist with 7 years of experience performed the imaging analysis. The size of tumor was evaluated on axial and coronal pre- and post- T1-weighted images. The axial images where maximal size of the tumor was depicted were used for measuring the largest dimension of anteroposterior (A) and mediolateral axis (B). The coronal images were used for the longest cranio-caudal axis length (C) of the tumor. The tumor volume was calculated by $\frac{4}{3} \pi \times \frac{1}{2} A \times \frac{1}{2} B \times \frac{1}{2} C$.

ADC analysis

ADC maps were constructed by a mono-exponential fitting model using available software (OleaSphere, Version 3.0; Olea Medical, La Ciotat, France). The 7-year-experienced radiologist carefully outlined each tumor of pre- and post-treatment status on axial post contrast T1-weighted images and transposed the freehand region of interest (ROI) to the ADC map. The ROIs were depicted on predominantly solid enhancing portions of tumors without cystic or necrotic areas on post-contrast T1-weighted images. Manually, the ROI spared the peripheral 2 mm of lesions to avoid volume averaging.¹² When geometric distortion was observed, the location and size were adjusted on ADC map in order for the ROI to be included within the tumor. An additional ROI was placed in the cervical spinal cord of the level of C2-C3 disc space as an internal standard, which was included in the field of view of every study.¹³ A normalized ADC ratio was calculated by dividing each mean ADC value of the lesion by the mean ADC value of the cervical cord in order to adjust for variation of ADC values among MRI scanners, magnetic field strengths, and matrix sizes.

Quantitative DCE analysis

All quantitative analyses in DCE-MRI were performed using OleaSphere 3.0 software permeability module which is based on the

extended Tofts model, by which pixel-based parameter maps are calculated from time intensity curves. The same radiologist depicted the ROI on each lesion of pre- and post-treatment status on the permeability maps, which predominantly showed enhancing components of tumors. The same radiologist placed an ROI on the external carotid artery of the affected side as arterial input function. The calculated quantitative parameters were Vp (blood plasma volume per unit tissue volume), Ve (extravascular, extracellular space (EES) volume per unit tissue volume), Kep (rate transfer constant between EES and blood plasma per minute), and Ktrans (volume transfer constant between EES and blood plasma per minute).

Statistical analysis

The mean ADC, normalized mean ADC values, Vp, Ve, Kep, and Ktrans were compared between pre-treatment status and post-treatment status by paired sample-test.

The Pearson correlation coefficient was used for the relationship between ratio of volume (post-treatment/pre-treatment status) and pre-treatment and post-treatment parameters. All statistical calculations were conducted with the statistical computing language R (version 4.0.4; R Foundation for Statistical Computing, Vienna, Austria). Variables with a $p < 0.05$ were considered as statistically significant.

RESULT

Patients' demographics

The patients' demographics, ADC values, and pre- and post-treatment perfusion values are summarized in Table 1. The patients were 55.2 ± 10.3 years (male: 2, female: 9). Nine lesions were located in the jugular fossa (right: 3, left: 6) and two lesions were located at the right carotid artery bifurcation. The median pre-treatment volume of the lesion was 13.52 cm³ (range: 3.78–171.1 cm³). The median volume change ratio (post-treatment status/pre-treatment status) was 0.80 (range: 0.47–1.53). Representative cases of size-controlled group and size-uncontrolled group are shown in Figures 1 and 2, respectively.

ADC values and quantitative DCE-MRI parameters analysis for pre- and post-treatment status

Pre- and post-treatment parameters are summarized in Table 2. Mean and normalized mean ADC values were significantly higher in post-treatment status than pre-treatment status (mean ADC: 1.25 ± 0.25 vs. 1.36 ± 0.20 × 10⁻³ mm²/s; $p = 0.005$, normalized mean ADC: 1.50 ± 0.33 vs. 1.81 ± 0.26; $p = 0.005$, respectively). The mean ADC value of the cervical cord as an internal standard was 0.77 ± 0.05 × 10⁻³ mm²/s. As for quantitative parameters, arterial input function curves



TABLE 1 Patients' demographics

Patient	Sex	Age	Location	RT	Pre-treatment volume (cm ³)	Post-treatment volume (cm ³)	Pre		Pre nADC/Post nADC	Pre Ve/Post Ve	Pre Kep/Post Kep	Pre Vp/Post Vp	Pre Ktrans/Post Ktrans
							ADC (×10 ⁻³ mm ² /s)	ADC (×10 ⁻³ mm ² /s)					
1	M	36	L jugular fossa	EBRT,45Gy/25Fr	7.07	4.88	1.38/1.53	1.84/2.04	0.67/0.42	1.65/0.91	0.16/0.33	1.44/0.31	
2	F	66	L jugular fossa	EBRT,50Gy/25Fr	4.85	4.03	1.35/1.53	1.80/2.04	0.57/0.21	6.78/4.21	0.30/0.30	1.68/0.95	
3	M	46	L jugular fossa	SRT,25Gy/5Fr	7.53	5.57	1.13/1.53	1.51/2.05	0.35/0.48	2.17/0.66	0.48/0.48	0.69/0.30	
4	F	59	L jugular fossa	EBRT,50.4Gy/28Fr	1.98	1.58	0.88/1.05	1.17/1.40	0.15/0.10	1.71/1.66	0.44/0.48	0.31/0.10	
5	F	53	R jugular fossa	EBRT,45Gy/25Fr	3.43	3.43	1.17/1/34	1.56/1.79	0.46/0.64	15.63/4.79	0.32/0.32	2.15/1.94	
6	F	61	R jugular fossa	EBRT,50Gy/25Fr	28.1	21.5	1.36/1.68	1.81/2.24	0.24/0.20	3.58/1.13	0.31/0.41	1.05/0.34	
7	F	54	L jugular fossa	EBRT,50Gy/25Fr	89.5	72.5	1.05/1.25	1.40/1.67	0.59/0.35	5.49/1.50	0.31/0.31	1.46/0.38	
8	F	42	R carotid bifurcation	EBRT,50Gy/25Fr	10.4	4.89	0.59/1.17	0.79/1.56	0.23/0.19	0.52/1.73	0.42/0.42	0.52/0.38	
9	F	58	L jugular fossa	SRT,30Gy/5Fr	2.66	2.66	1.36/1.12	1.81/1.49	0.54/0.20	3.53/0.95	0.31/0.36	1.44/0.17	
10	F	63	R carotid bifurcation	SRT,30Gy/5Fr	12.31	8.12	0.91/1.37	1.21/1.83	0.76/0.43	2.58/0.81	0.15/0.15	1.46/0.27	
11	F	69	R jugular fossa	EBRT,45Gy/25Fr	2.13	3.26	1.20/1.35	1.60/1.80	0.24/0.37	8.39/7.44	0.34/0.36	2.33/2/94	

Abbreviations: ADC, apparent diffusion coefficient; EBRT, external beam radiation therapy; F, female; Fr, fractions; Gy, gray; Kep, rate transfer constant between EES and blood plasma per minute; Ktrans, volume transfer constant between EES and blood plasma per minute; L, left; M, male; R, right; RT, radiation therapy; SRT, stereotactic radiotherapy; Ve, extravascular, extracellular space (EES) volume per unit tissue volume; Vp, blood plasma volume per unit tissue volume.

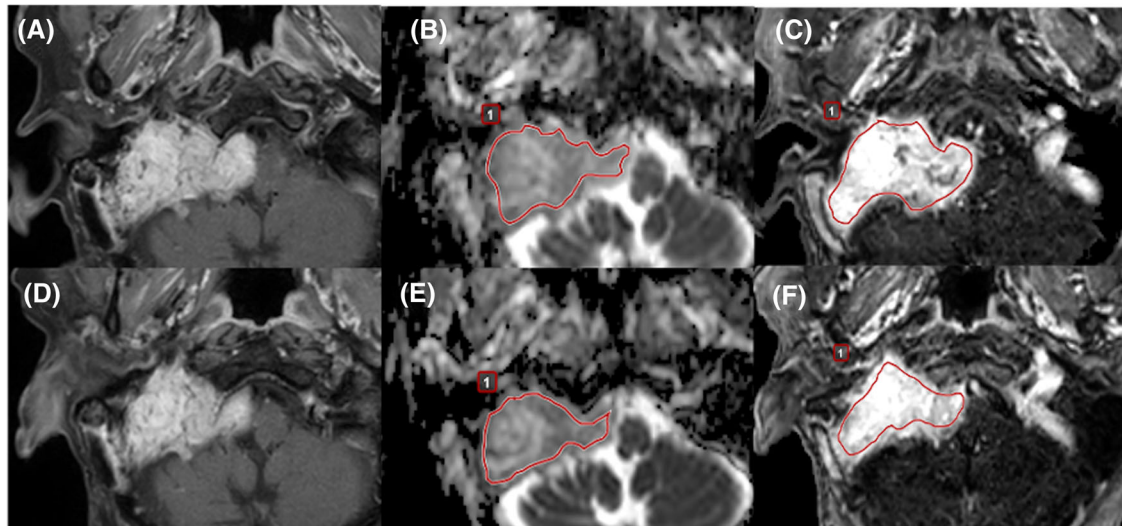


FIGURE 1 A 61-year-old male with paraganglioma in the right jugular foramen. (A) Post-contrast T1-weighted image, (B) apparent diffusion coefficient (ADC) map, and (C) permeability map demonstrate a pre-treatment paraganglioma in the right jugular foramen. (D) Post-contrast T1-weighted image, (E) ADC map, and (F) permeability map demonstrate a post-treatment paraganglioma. A freehand region of interest (ROI) is placed on (B) and (E) ADC maps, and pre- and post-treatment ADC values are calculated. Another freehand ROI is placed on (C) and (F) permeability maps, and quantitative parameters are calculated. In this case, the tumor regresses after external beam radiation therapy

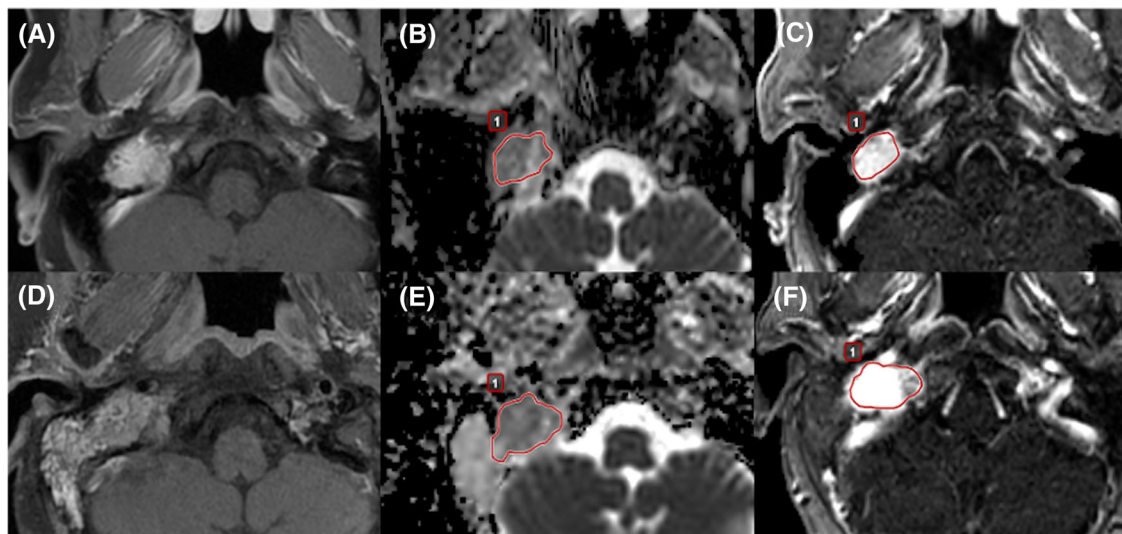


FIGURE 2 A 69-year-old female with paraganglioma in the right jugular foramen. (A) Post-contrast T1-weighted image, (B) apparent diffusion coefficient (ADC) map, and (C) permeability map demonstrate a pretreatment paraganglioma in the right jugular foramen. (D) Post-contrast T1-weighted image, (E) ADC map, and (F) permeability map demonstrate a post-treatment paraganglioma. A freehand region of interest (ROI) is placed on (B) and (E) ADC maps, and pre- and post-treatment ADC values are calculated. Another freehand ROI is placed on (C) and (F) permeability maps, and quantitative parameters are calculated. In this case, the tumor grows after external beam radiation therapy. In addition, the tumor invades the right mastoid air cells and results in opacification

showed a pulsed input pattern in all examination. K_{trms} and K_{ep} were significantly lower in post-treatment status than in pre-treatment status (K_{trms} (min^{-1}): 1.32 ± 0.64 vs. 0.73 ± 0.89 ; $p = 0.007$, K_{ep} (min^{-1}): 4.82 ± 4.31 vs. 2.34 ± 2.18 ; $p = 0.027$, respectively). V_p and V_e were not significantly different between pre- and post-treatment status. Representative cases of size-controlled group and size-uncontrolled group are shown in Figures 1 and 2, respectively.

Relationship between tumor volume ratio (post-treatment status/pre-treatment status) and pre-treatment and post-treatment parameters

The tumor volume ratio (post-treatment status/pre-treatment status) and pre-treatment parameters are summarized in Table 3. The correlation coefficient of K_{trms} was statistically significant ($r = 0.70$;

TABLE 2 ADC values and quantitative parameters between pre- and post-treatment status

	Pre-treatment status	Post-treatment status	p-value
Mean ADC value($\times 10^{-3}$ mm ² /s)	1.25 \pm 0.25	1.36 \pm 0.20	0.005
Normalized mean ADC value	1.50 \pm 0.33	1.81 \pm 0.26	0.005
Vp	0.32 \pm 0.10	0.36 \pm 0.09	0.07
Ve	0.44 \pm 0.21	0.33 \pm 0.16	0.10
Kep (min ⁻¹)	4.82 \pm 4.31	2.34 \pm 2.18	0.027
Ktrans (min ⁻¹)	1.32 \pm 0.64	0.73 \pm 0.89	0.007

Note: Values are described as mean \pm standard deviation.

Abbreviations: ADC, apparent diffusion coefficient; Kep, rate transfer constant between EES and blood plasma per minute; Ktrans, volume transfer constant between EES and blood plasma per minute; Ve, extravascular, extracellular space (EES) volume per unit tissue volume; Vp, blood plasma volume per unit tissue volume.

TABLE 3 Relationship of ratio of volume (post-treatment status/pre-treatment status) and pre-treatment parameters

	Mean ADC value	Normalized mean ADC value	Vp	Ve	Kep	Ktrans
Correlation coefficient (<i>r</i>)	0.42, 95% CI (0.25-0.81)	0.42, 95% CI (0.25-0.81)	0.036, 95% CI (-0.58 to 0.62)	-0.19, 95% CI (-0.71 to 0.46)	0.59, 95% CI (0.02-0.88)	0.70, 95% CI (0.18-0.92)
p-value	0.20	0.20	0.92	0.58	0.058	0.016

Abbreviations: ADC, apparent diffusion coefficient; CI, confidence intervals; Kep, rate transfer constant between EES and blood plasma per minute; Ktrans, volume transfer constant between EES and blood plasma per minute; Ve, extravascular, extracellular space (EES) volume per unit tissue volume; Vp, blood plasma volume per unit tissue volume.

$p = 0.016$) (Figure 3). The relationship between the volume ratio and other pretreatment parameters was not shown to be significantly different.

The tumor volume ratio (post-treatment status/pre-treatment status) and post-treatment parameters are summarized in Table 4. The correlation coefficient of Ktrans and Kep was statistically significant ($r = 0.83$; $p = 0.002$, $r = 0.8$; $p = 0.003$, respectively) (Figure 3). The relationship between the volume ratio and other post-treatment parameters is not shown to be significantly different.

DISCUSSION

This study was designed to explore diffusion and perfusion values for detection of the response to RT of head and neck paragangliomas. In our study, mean and normalized mean ADC values were significantly higher in post-treatment status than in pre-treatment status. Ktrans and Kep were significantly lower in post-treatment status than in pre-treatment group. The tumor volume ratio and pre-treatment Ktrans, and the tumor volume ratio and post-treatment Ktrans and Kep were correlated with significant difference. Our result implies that paragangliomas with higher Ktrans tend to grow after the RT, and Ktrans can be a surrogate to predict tumor response to RT. ADC values showed significant difference between pre- and post-treatment status, but the pre- and post-treatment ADC values did not show a relationship with tumor volume ratio.

DCE-MRI enables noninvasive evaluation of the tumor microvascular environment with quantitative analysis of the permeability parameters. It has been proposed that Ktrans and Kep can reflect the microvascular permeability of the tumor.^{14,15} Paragangliomas can show different tumor cell morphology, cellularity, and various histological patterns, such as nests of tumor cells separated by peripheral capillaries (zellballen pattern), or large and irregular cell nest pattern.^{16,17} Therefore, the parameters related to permeability may vary depending on the various pathologic backgrounds. For example, when paragangliomas demonstrate zellballen pattern accompanied by peripheral capillaries, which function as arteriovenous shunt, gadolinium contrast does not leak into EES, which result in low permeability. Given our result of relationship between the tumor's volume and pre-treatment Ktrans, and pathologic backgrounds of head and neck paragangliomas, it is indicated that the paragangliomas with the pathological features which show high permeability even after RT lead to tumor growth. Moreover, our result suggested that the tumors with large residual size did not necessarily show higher perfusion parameters, which may imply that the residual size tumor volume does not affect the perfusion parameters.

We evaluated the ADC values on a single axial slice instead of the entire tumor volume because prior studies using volumetric ADC analyses showed no better ability than single axial section evaluations.^{18,19} Additionally, we also performed normalized ADC values to those of the cervical spinal cord to minimize variations due to magnetic field differences. Given our strategy for standardization, we believe that our

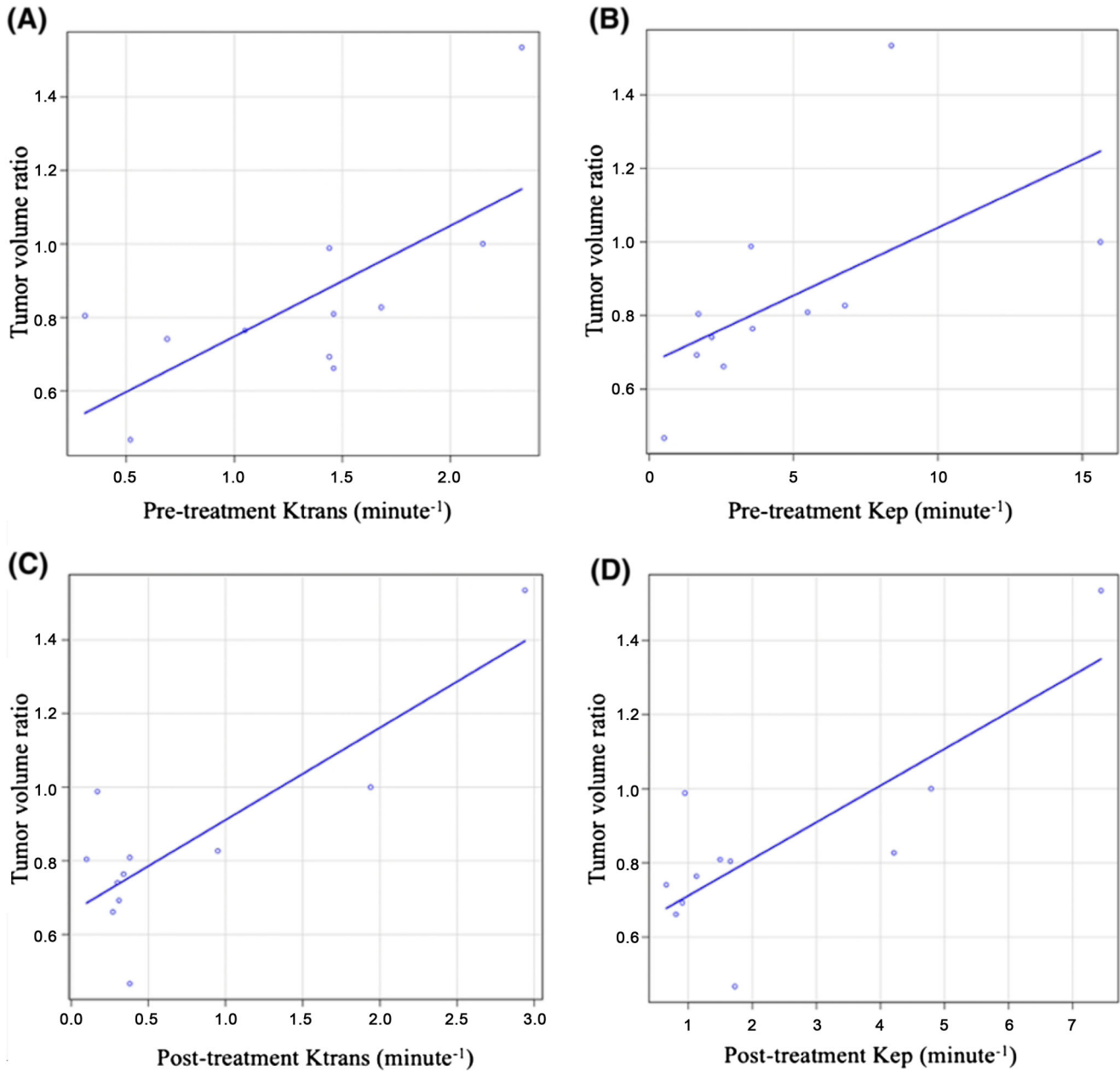


FIGURE 3 (A) and (B) show the regression lines of the relationship between tumor volume ratio (post-treatment status/pre-treatment status) and pre-treatment Ktrms (volume transfer constant between extravascular, extracellular space [EES] and blood plasma per minute) and Kep (rate transfer constant between EES and blood plasma per minute) ($r = 0.70$; $p = 0.016$, $r = 0.59$; $p = 0.058$, respectively). (C) and (D) show the regression lines of the relationship between tumor volume ratio and post-treatment Ktrms and Kep ($r = 0.83$; $p = 0.002$, $r = 0.8$; $p = 0.003$, respectively)

TABLE 4 Relationship of ratio of volume (post-treatment status/pre-treatment status) and post-treatment parameters

	Mean ADC value	Normalized mean ADC value	Vp	Ve	Kep	Ktrms
Correlation coefficient (r)	-0.06, 95% CI (-0.64 to 0.56)	-0.06, 95% CI (-0.64 to 0.56)	-0.017, 95% CI (-0.61 to 0.59)	0.19, 95% CI (-0.46 to 0.71)	0.8, 95% CI (0.37-0.94)	0.83, 95% CI (0.45-0.95)
p -value	0.87	0.86	0.96	0.58	0.003	0.002

Abbreviations: ADC, apparent diffusion coefficient; CI, confidence intervals; Kep, rate transfer constant between EES and blood plasma per minute; Ktrms, volume transfer constant between EES and blood plasma per minute; Ve, extravascular, extracellular space (EES) volume per unit tissue volume; Vp, blood plasma volume per unit tissue volume.

results can be validated and robust. Based on our result, ADC values significantly increased between pre- and post-treatment status without clear relationship with the tumor's volume. Increase of ADC values may represent decrease of cellularity due to RT-related change. A previous study for head and neck malignant tumor showed that ADC can be used as an effective parameter for prediction and early detection of response to RT.⁸ According to our study, it may be postulated that paragangliomas with high permeability can grow even though cellularity is reduced after RT. As for paragangliomas, permeability parameters of DCE-MRI can be a more reliable noninvasive marker to predict response to RT than ADC values. In our study, the statistical analysis for cutoff value analysis of prediction of the outcome of RT, such as tumor regression or tumor growth, was not performed due to a small cohort. The research about the prediction value is clinically important and expected to be performed with larger study population in the future.

As for tumor volume approximation, we applied three perpendicular dimensions based on the assumption that the tumor is an ellipsoid shape, as previous studies performed.²⁰⁻²² This approximation is easy to apply in clinical practice because of its simplicity. Therefore, this volume approximation seems to be a standard in the case of head and neck paragangliomas, which are ellipsoid shaped in most cases.

This study has several limitations. First, this was a retrospective study with a small cohort of patients from a single institution. Second, statistical analysis using cases with histological confirmation cannot be performed due to the small number of cases. We also included the patients who were not evaluated histopathologically, but were diagnosed based on accepted and established diagnostic tests, such as elevated plasma or urinary fractionated metanephrines, imaging findings of head and neck CT and MRI, positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro-D-glucose integrated with CT and ¹¹¹In-pentetreotide single-photon emission CT.^{1,4,23,24} Third, DCE-MRI was performed using both 1.5T and 3T scanners.

In conclusion, Ktrans has a predictive potential to predict the response to RT of head and neck paragangliomas in this pilot study.

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