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Comparative Prognostic Value of 11 C-Methionine and 18 F-FDG PET/CT for Tumor Progression and Hearing Deterioration in NF2-Related Vestibular Schwannomas

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Research Article

Keywords: NF2-related schwannomatosis, vestibular schwannoma, 11C-methionine, 18F-fluorodeoxyglucose, positron emission tomography/computed tomography

Posted Date: September 27th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10987451/v1

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Additional Declarations: No competing interests reported.

Abstract

Purpose.

To compare the metabolic imaging characteristics and prognostic value of ^{11}C-methionine and ^{18}F-fluorodeoxyglucose PET/CT in NF2-related vestibular schwannomas.

Methods.

This single-center retrospective cohort included 22 adults with 40 untreated vestibular schwannomas who underwent baseline ^{11}C-MET and ^{18}F-FDG PET/CT and audiological assessment. Median follow-up was 21 months. Tracer uptake and tumor-to-cerebellum ratios were compared. Receiver operating characteristic and Cox regression analyses evaluated associations with volumetric tumor progression and hearing deterioration.

Results.

Although maximum standardized uptake value (SUVmax) was higher with ^{18}F-FDG than with ^{11}C-MET (3.69 ± 1.12 vs 3.08 ± 0.83; P < .001), maximum tumor-to-background ratio (TBRmax) was substantially higher with ^{11}C-MET (2.43 ± 0.59 vs 0.54 ± 0.14; P < .0001). For predicting tumor progression, ^{11}C-MET TBRmax achieved an area under the curve of 0.753, compared with 0.507 for ^{18}F-FDG TBRmax (P = .02). Corresponding values for hearing deterioration were 0.736 and 0.531. In multivariable analysis, ^{11}C-MET TBRmax independently predicted tumor progression (hazard ratio, 2.958; 95% confidence interval, 1.380–6.339; P = .0053) and hearing deterioration (hazard ratio, 3.223; 95% confidence interval, 1.021–10.172; P = .046). No ^{18}F-FDG-derived parameter was significantly associated with either outcome.

Conclusion.

^{11}C-MET PET/CT provided superior tumor-to-background contrast and stronger prognostic information than ^{18}F-FDG PET/CT in NF2-related vestibular schwannomas. These findings support prospective evaluation of ^{11}C-MET TBRmax as an imaging biomarker for individualized surveillance.

Introduction

NF2-related schwannomatosis (NF2-SWN), formerly known as neurofibromatosis type 2, is an autosomal dominant disorder characterized by multiple tumors of the nervous system. Bilateral vestibular schwannomas (VSs) are the hallmark manifestation [1], [2]of the disease and represent one of the major causes of hearing impairment and reduced quality of life in affected patients. NF2-related VSs may lead to sensorineural hearing loss, tinnitus, vestibular dysfunction, and brainstem compression. Current management strategies include active surveillance, microsurgical resection, radiotherapy, and anti-angiogenic or other systemic therapies. Because patients with NF2-SWN often present with multifocal disease, a long clinical course, and substantial interpatient and intertumoral heterogeneity, balancing tumor control with preservation of hearing, facial nerve function, and quality of life [2, 3] remains a central challenge in clinical decision-making. Previous studies have suggested that clinical factors such as sex, age at onset, family history, symptom duration, and baseline hearing status may help assess disease burden or severity [4, 5]; however, their ability to predict long-term tumor progression and hearing trajectories remains limited. Therefore, imaging or molecular biomarkers that reflect tumor biological activity and assist in predicting hearing outcomes are urgently needed to optimize individualized management for patients with NF2-SWN [6–9].

MRI is the cornerstone imaging modality for the diagnosis, surveillance, and treatment planning of patients with NF2-SWN. It provides detailed information on the anatomical location of VSs, tumor size, internal auditory canal involvement, and brainstem compression. However, conventional MRI primarily depicts morphological changes and has limitations in predicting tumor metabolic activity, underlying growth kinetics, and future changes in hearing function. PET/CT may provide complementary information to MRI by capturing tracer uptake associated with tumor-related pathophysiological processes. ^{18}F-FDG is the most widely used oncologic PET tracer; however, in brain lesions and tumors located in the cerebellopontine angle region, high physiological glucose uptake in the normal brain parenchyma and cerebellum reduces tumor-to-background contrast, thereby limiting lesion visualization and quantitative assessment of benign intracranial neurogenic tumors [10, 11]. In contrast, amino acid tracers such as ^{11}C-MET show relatively low uptake in normal brain tissue [12–14] and can therefore provide higher tumor-to-background contrast. ^{11}C-MET uptake may reflect biological processes such as amino acid transport, protein synthesis demand, and tumor cell activity. Previous studies in brain tumors have shown that ^{11}C-MET PET may outperform ^{18}F-FDG PET in lesion visualization [15, 16], metabolic activity assessment, and target delineation for selected intracranial lesions. However, in NF2-related VSs, systematic comparisons of the metabolic profiles and quantitative parameters of ^{11}C-MET and ^{18}F-FDG PET/CT, as well as their associations with tumor progression and hearing outcomes, remain limited [14–16].

In this single-center retrospective cohort study, we aimed to directly compare the metabolic imaging characteristics of ^{11}C-MET and ^{18}F-FDG PET/CT in NF2-related VSs and to evaluate the associations between PET-derived quantitative parameters, tumor progression, and hearing deterioration. The specific objectives were: (1) to compare tracer uptake levels and tumor-to-background contrast between ^{11}C-MET and ^{18}F-FDG in NF2-related VSs; (2) to assess the ability of ^{11}C-MET and ^{18}F-FDG PET/CT parameters to predict tumor progression and hearing deterioration; and (3) to explore potential predictors of progression-free survival and hearing preservation time by integrating clinical and conventional imaging variables. We hypothesized that, compared with ^{18}F-

FDG, ^{11}C-MET would provide higher tumor-to-background contrast and may offer additional functional imaging information for risk stratification in NF2-related VSs.

Materials and Methods

Study Population and Study Design

This retrospective clinical cohort study included patients with NF2-related vestibular schwannomas (VSs) who were managed at Beijing Tiantan Hospital between January 2014 and December 2018. All patients underwent both ^{11}C-methionine (^{11}C-MET) and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT imaging, as well as audiological assessment at baseline. Patients were followed for at least 6 months to evaluate tumor progression and hearing outcomes. The primary analysis focused on untreated ears, with a total of 40 ears included. Each ear was analyzed as an observational unit. This study was approved by the Ethics Committee of Beijing Tiantan Hospital (approval number: KY2024-280-02).

Patients were eligible if they met the following criteria:a clinical diagnosis of NF2, defined as bilateral VSs or unilateral VS with a first-degree family history of NF2 and other NF2-associated tumors; age ≥ 18 years and no prior treatment directed at the target VS, including surgery, radiotherapy, or bevacizumab;preserved measurable hearing at baseline, defined as a pure-tone average (PTA) ≤ 70 dB.Patients were excluded if they had any of the following: pregnancy or renal insufficiency, defined as an estimated glomerular filtration rate (eGFR) < 45 mL/min; a history of otologic surgery, except for diagnostic biopsy; coexisting hearing-loss disorders unrelated to VS, such as noise-induced hearing loss or Ménière's disease. A total of 22 patients involving 40 ears were included in the final analysis.

Audiological Assessment

Audiological assessments were performed every 6 months and included the following parameters. The word recognition score (WRS) was defined as the percentage of correctly recognized monosyllabic words. Standardized audiological testing procedures were used to minimize the potential influence of retrocochlear dysfunction and the rollover phenomenon. The pure-tone average (PTA) was calculated as the average air-conduction threshold at 500, 1000, 2000, and 4000 Hz and was expressed in decibels (dB). Hearing status was classified according to the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) criteria. Class A was defined as PTA ≤ 30 dB and WRS > 70%, and Class B as PTA > 30–50 dB and WRS ≥ 50%; Classes A and B were considered serviceable hearing. Class C was defined as PTA > 50 dB and WRS ≥ 50%, and Class D as any PTA with WRS < 50%; Classes C and D were considered non-serviceable hearing.The endpoint event for hearing deterioration was defined as an increase in PTA of ≥ 10 dB or a decrease in WRS of ≥ 15% from baseline.

PET/CT Imaging

^{11}C-methionine (^{11}C-MET) was synthesized in-house using a Zymark robotic system. Briefly, L-homocysteine thiolactone was loaded onto a C^{18} cartridge in a NaOH/ethanol solution. After the introduction of ^{11}C-methyl iodide, the product was eluted with phosphate buffer and passed through a sterile filter. The final product met radiopharmaceutical quality-control standards, including radiochemical purity > 95%, specific activity > 10,000 GBq/mmol, sterility, absence of pyrogens, pH 4.5–8.5, ethanol content < 3.5%, D/L ratio > 90%, and osmolality of 200–800 mOsm/kg. The synthesis success rate was > 95%. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) was prepared according to standard clinical procedures, with radiochemical purity > 99%. The injected dose of ^{18}F-FDG was 3.7 MBq/kg, and the injected dose of ^{11}C-MET was 370 MBq [17, 18]. PET/CT acquisition was initiated 60 minutes after ^{18}F-FDG injection and 20 minutes after ^{11}C-MET injection. Low-dose CT was performed for attenuation correction using the following parameters: 120 kV and 30 mAs. Images were analyzed on a Siemens SyngoVia 24B workstation by two nuclear medicine physicians independently. The maximum standardized uptake value (SUVmax) and mean standardized uptake value (SUVmean) of each tumor were recorded. The tumor-to-background ratio (TBR) was calculated using the contralateral cerebellum as the reference brain region. All PET data were reconstructed using an iterative ordered-subset expectation maximization (OSEM) algorithm to ensure image consistency. Tumor size was assessed on MRI by measuring the greatest diameter (GD). Regions of interest (ROIs) were delineated by an experienced neuroradiologist.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 and R version 4.3.3. Categorical variables are presented as frequencies, and continuous variables are presented as mean ± standard deviation. A two-sided P value < 0.05 was considered statistically significant. Kendall's τ test was used to assess the correlations of clinical variables and PET/CT parameters derived from ^{11}C-MET and ^{18}F-FDG with tumor progression and hearing deterioration. Differences in tracer uptake parameters between ^{11}C-MET and ^{18}F-FDG PET/CT were analyzed using the Wilcoxon signed-rank test. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of FDG-SUVmax tumor-to-cerebellum ratio to distinguish serviceable from non-serviceable hearing. For survival analysis, Kaplan–Meier curves were generated to evaluate the associations of ^{11}C-MET and ^{18}F-FDG PET/CT parameters with tumor progression and loss of serviceable hearing. Differences between groups were assessed using the log-rank test. Univariable and multivariable Cox proportional hazards regression models were used to evaluate the associations of clinical and imaging variables with progression-free survival (PFS) and hearing deterioration-free survival (HFS) in patients with vestibular schwannoma. Potential predictors were first screened using univariable analysis, and variables with P < 0.05 in univariable analysis were subsequently included in the multivariable model to identify independent prognostic predictors. Hazard ratios (HRs) and 95% confidence intervals (CIs) were used to quantify the strength of association. A P value < 0.05 was considered statistically significant.

Results

Patient Characteristics and Univariable Analysis

This retrospective study included 40 vestibular schwannomas (VSs) from 22 patients with neurofibromatosis type 2 (NF2). All patients underwent baseline ^{11}C-MET PET/CT and ^{18}F-FDG PET/CT examinations. The clinical and demographic characteristics of the study population are summarized in Table 1. According to the diagnostic criteria for NF2, all patients had bilateral VSs. The median clinical follow-up was 21 months (range, 9–36 months).Representative baseline PET and longitudinal MRI findings are shown in Fig. 1.

Table 1
Baseline Demographic and Clinical Characteristics of the Study Population

			Tumor Progression			Hearing Progression		
	level	Overall	0	1	P-Value	0	1	P-Value
N=		40	15	25		16	24	
Age(mean (SD))		24.23 (6.57)	24.13 (6.71)	24.28 (6.62)	0.947	23.40 (4.91)	24.72 (7.44)	0.545
Family History (%)	0	38 (95.0)	14 (93.3)	24 (96.0)	1	15 (100.0)	23 (92.0)	0.708
	1	2 (5.0)	1 (6.7)	1 (4.0)		0 (0.0)	2 (8.0)	
Course of Disease (mean (SD))		89.55 (49.52)	94.87 (50.58)	86.36 (49.63)	0.605	76.93 (40.58)	97.12 (53.52)	0.216
Tumor Volume(mean (SD))		4.16 (4.34)	2.85 (2.82)	4.95 (4.92)	0.139	2.55 (2.44)	5.14 (4.95)	0.067
Annual Rate of Increase (mean (SD))		1.30 (2.04)	0.81 (0.87)	1.61 (2.49)	0.296	0.39 (0.43)	1.87 (2.43)	0.047
V*Mean (mean (SD))		7.90 (7.61)	4.91 (5.29)	9.70 (8.29)	0.052	4.78 (4.67)	9.78 (8.46)	0.043
METSUVmax (mean (SD))		3.08 (0.83)	2.78 (0.62)	3.26 (0.89)	0.077	2.93 (0.66)	3.17 (0.91)	0.378
METSUVmaxT/C (mean (SD))		2.43 (0.59)	2.12 (0.37)	2.63 (0.62)	0.007	2.14 (0.43)	2.61 (0.61)	0.012
FDGSUVmax (mean (SD))		3.69 (1.12)	3.67 (1.19)	3.71 (1.10)	0.926	3.74 (1.28)	3.67 (1.03)	0.846
FDGSUVmaxT/C (mean (SD))		0.54 (0.14)	0.54 (0.14)	0.54 (0.14)	0.924	0.53 (0.13)	0.55 (0.15)	0.784
Hypermetabolism(%)	0	7 (17.5)	2 (13.3)	5 (20.0)	0.914	4 (26.7)	3 (12.0)	0.452
	1	33 (82.5)	13 (86.7)	20 (80.0)		11 (73.3)	22 (88.0)	
Cystic change (%)	0	28 (70.0)	13 (86.7)	15 (60.0)	0.154	12 (80.0)	16 (64.0)	0.476
	1	12 (30.0)	2 (13.3)	10 (40.0)		3 (20.0)	9 (36.0)	
Lobulation (%)	0	18 (45.0)	5 (33.3)	13 (52.0)	0.412	8 (53.3)	10 (40.0)	0.622
	1	22 (55.0)	10 (66.7)	12 (48.0)		7 (46.7)	15 (60.0)	

Univariable analysis showed that the maximum tumor-to-background ratio measured on MET PET/CT (MET-TBRmax) was significantly associated with volumetric tumor progression ($P < 0.05$). Tumor annual growth rate, metabolic tumor volume measured on MET PET/CT, and MET-TBRmax were significantly associated with hearing deterioration ($P < 0.05$). In contrast, none of the ^{18}F-FDG PET/CT-derived parameters showed statistically significant associations with these outcomes.

Comparison of ^{11}C-MET and ^{18}F-FDG PET/CT Uptake and Predictive Performance

The maximum standardized uptake value (SUVmax) was higher on ^{18}F-FDG PET/CT than on ^{11}C-MET PET/CT (3.69 ± 1.12 vs. 3.08 ± 0.83, $P < 0.001$). However, the mean MET-TBRmax was significantly higher than the FDG-TBRmax (2.43 ± 0.59 vs. 0.54 ± 0.14, $P < 0.0001$).

Receiver operating characteristic (ROC) curve analysis showed that a MET-TBRmax cutoff value of ≥ 2.410 yielded an area under the curve (AUC) of 0.753 for predicting volumetric tumor progression. In comparison, an FDG-TBRmax cutoff value of > 0.496 yielded an AUC of 0.507. MET-TBRmax showed significantly better predictive performance for volumetric tumor progression than FDG-TBRmax ($P = 0.02$)(Fig. 2).

For hearing deterioration, a MET-TBRmax cutoff value of ≥ 2.295 yielded an AUC of 0.736, whereas an FDG-TBRmax cutoff value of > 0.583 yielded an AUC of 0.531. MET-TBRmax showed better predictive performance for hearing deterioration than FDG-TBRmax.

Survival and Prognostic Analyses

Kaplan–Meier survival curves and log-rank tests were used to evaluate the prognostic value of PET-derived parameters for progression-free survival (PFS) and hearing preservation survival (HFS). Kaplan–Meier analysis showed that the high MET-TBRmax group had significantly shorter median time to volumetric

tumor progression and hearing loss. In contrast, no statistically significant difference in tumor progression was observed in the high FDG-TBRmax group (P = 0.14)(Fig. 3).

In the analysis of tumor progression, univariable Cox regression identified the following variables as significantly associated with an increased risk of progression: cystic change (HR = 2.257, 95% CI 1.007–5.058, P = 0.048), mean tumor enhancement value (VMean; HR = 1.060, 95% CI 1.008–1.115, P = 0.0225), and MET PET-derived tumor-to-cerebellum ratio (MET-TBRmax; HR = 3.503, 95% CI 1.726–7.110, P = 0.0005). After adjustment for potential confounders in multivariable analysis, only MET-TBRmax remained an independent predictor of tumor progression (HR = 2.958, 95% CI 1.380–6.339, P = 0.0053). Cystic change (P = 0.3932) and VMean (P = 0.1473) did not retain independent prognostic significance.

In the analysis of hearing deterioration, univariable Cox regression showed that VMean (HR = 1.051, 95% CI 1.003–1.102, P = 0.0383), annual rate of increase (HR = 1.234, 95% CI 1.038–1.468, P = 0.0174), MET-SUVmax (HR = 1.821, 95% CI 1.082–3.065, P = 0.0241), and MET-TBRmax (HR = 4.298, 95% CI 2.048–9.022, P = 0.0001) were significantly associated with an increased risk of hearing deterioration. In multivariable analysis, only MET-TBRmax remained an independent predictor of hearing deterioration (HR = 3.223, 95% CI 1.021–10.172, P = 0.046). Annual rate of increase (P = 0.9882) and VMean (P = 0.527) were not independently significant in the multivariable model.The results of the univariable and multivariable Cox regression analyses are summarized in Table 2.

Table 2
Univariate and multivariate Cox regression of Tumor Progress and Hearing Loss

Variable	Tumor Progress							Hearing Loss				
	HR	CI_lower	CIupper	P_value	HR	HR_95CI	P_value	HR	CI_lower	CLupper	P_value	HR
Family History	0.731	0.099	5.408	0.7589				1.646	0.38	7.12	0.5049	
Course of Disease	0.999	0.99	1.007	0.7369				1.005	0.998	1.013	0.1662	
Hypermetabolism	0.614	0.23	1.641	0.3309				1.845	0.551	6.179	0.3208	
Cystic change	2.257	1.007	5.058	0.048	1.462	0.611–3.499	0.3932	2.022	0.889	4.602	0.0932	
Lobulation	0.719	0.327	1.579	0.4108				1.428	0.64	3.186	0.3845	
VMean	1.060	1.008	1.115	0.0225	1.04	0.986–1.098	0.1473	1.051	1.003	1.102	0.0383	1.0
Tumor Volume	1.072	0.99	1.161	0.0883				1.062	0.988	1.142	0.1017	
Annual Rate of Increase	1.192	0.97	1.466	0.0953				1.234	1.038	1.468	0.0174	1.0
METSUVmax	1.941	1.172	3.215	0.01				1.821	1.082	3.065	0.0241	
METSUVmaxTC	3.503	1.726	7.11	0.0005	2.958	1.38–6.339	0.0053	4.298	2.048	9.022	0.0001	3.2
FDGSUVmax	1.038	0.724	1.487	0.8387				1.019	0.717	1.448	0.917	
FDGSUVmaxTC	2.080	0.125	34.562	0.6095				4.066	0.24	68.89	0.3312	

HR, hazard ratio; CI, confidence interval; MET, methionine; FDG, fluorodeoxyglucose; SUVmax, maximum standardized uptake value; TBRmax, maximum tum

Discussion

In this retrospective cohort of NF2-related vestibular schwannomas (VSs), ^{11}C-MET PET/CT provided substantially higher tumor-to-background contrast than ^{18}F-FDG PET/CT. MET-TBRmax was independently associated with both volumetric tumor progression and hearing deterioration after adjustment for clinical and imaging variables. By contrast, FDG-derived parameters showed limited discriminatory performance and no consistent associations with these outcomes in Cox regression analyses. These findings suggest that MET-TBRmax may provide information on tumor activity beyond conventional anatomical and growth-related imaging measures.

The difference between the tracers is biologically plausible. High physiological FDG uptake in the cerebral cortex and cerebellum reduces lesion-to-background contrast in the cerebellopontine angle. Furthermore, FDG uptake in benign schwannomas may be influenced by cellular composition, cystic change, inflammation, and vascular permeability, limiting its specificity for tumor progression [13, 14]. In contrast, ^{11}C-MET reflects amino acid transport and protein synthesis and has relatively low uptake in normal brain tissue [10–12]. Previous studies have shown improved visualization of acoustic neuromas and vestibular schwannomas with MET compared with FDG [15, 16]. The present findings extend these observations by demonstrating an association between MET-TBRmax and longitudinal tumor and hearing outcomes.

Cystic change, mean tumor enhancement, and annual growth rate were associated with outcomes in univariable analyses, but MET-TBRmax remained independently associated with both endpoints in the multivariable models. MET PET/CT may therefore complement serial MRI and audiological assessment by identifying lesions with relatively high metabolic activity. This information could support risk-adapted surveillance, particularly in patients with multiple

tumors. However, the present study does not establish that MET-guided intervention improves clinical outcomes; treatment decisions should continue to incorporate serial tumor measurements, hearing trajectories, symptoms, and patient preferences.

Clinical implementation of ^{11}C-MET PET/CT also presents practical limitations. The short physical half-life of ^{11}C requires access to an on-site or nearby cyclotron, radiochemical synthesis facilities, and appropriate quality-control systems. Its use may therefore initially be limited to specialized neuro-oncology or regional referral centers.

This study has several limitations. Its retrospective, single-center design and small sample size limit generalizability and may produce unstable estimates of optimal TBRmax thresholds. The relatively limited follow-up may not capture the intermittent or nonlinear growth patterns of NF2-related VSs. In addition, the inclusion of multiple tumors from individual patients may introduce within-patient correlation and should be considered in the statistical analysis. Finally, the absence of histological or molecular correlates prevents conclusions regarding the biological mechanisms underlying increased MET uptake. Prospective multicenter studies incorporating standardized PET acquisition, volumetric MRI, longitudinal audiological assessment, and appropriate adjustment for patient-level clustering are required to validate the prognostic value and clinical utility of MET-TBRmax.

Conclusion

In conclusion, ^{11}C-MET PET/CT provided higher tumor-to-background contrast than ^{18}F-FDG PET/CT, and MET-TBRmax was independently associated with tumor progression and hearing deterioration in NF2-related vestibular schwannomas. Prospective multicenter studies are warranted to validate MET-TBRmax as an adjunct to MRI-based surveillance and treatment planning.

Declarations

Authors contributed equally to this work and should be considered co-corresponding authors.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Tiantan Hospital (approval No. KY2024-280-02).

Consent to Participate

The requirement for informed consent was waived because of the retrospective study design.

Funding

This work was supported by the Beijing Science and Technology Plan Project (Z221100007422041) and National Natural Science Foundation of China (82304925).

Author Contribution

S.L. and L.A. designed the study. Y.G., Z.B., Y.H., and Z.C. acquired the data. S.L., X.Z., and Y.G. analyzed the data. S.L. and P.L. drafted the manuscript. All authors critically reviewed and revised the manuscript and approved the final version.

Acknowledgments.

The authors thank NF2-SWN patients for providing valuable data.

Data Availability

The data that support the findings of this study are available from the corresponding author, Pinan Liu, upon reasonable request.

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Figures

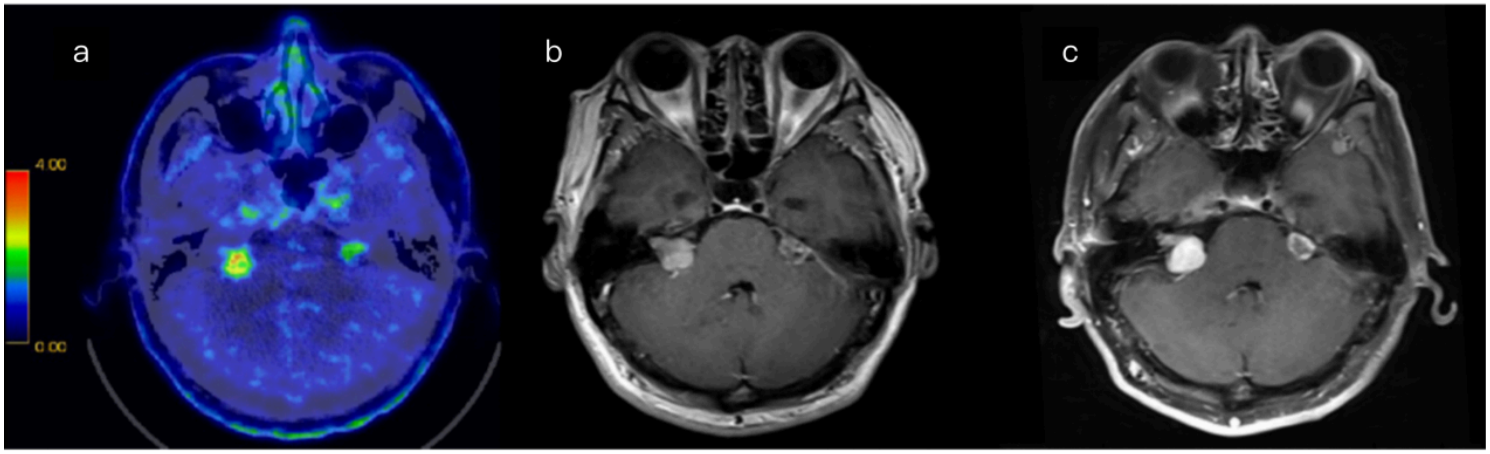


Figure 1

Representative imaging for NF2-associated VSs. (a): MET PET imaging showing a high TBRmax (TBRmax=3.4) right-sided lesion while a low TBRmax (TBRmax=2.2) lesion on left side. (b): The first MRI examination compared to MET PET at the same time. (c): The second MRI scan at least 6 months later showing a right sided growing VS (tumor growth rate=3mm/year) corresponding with high TBRmax while a static and cystic VS (tumor growth rate=0mm/year) on the opposite side by comparison of panel b.

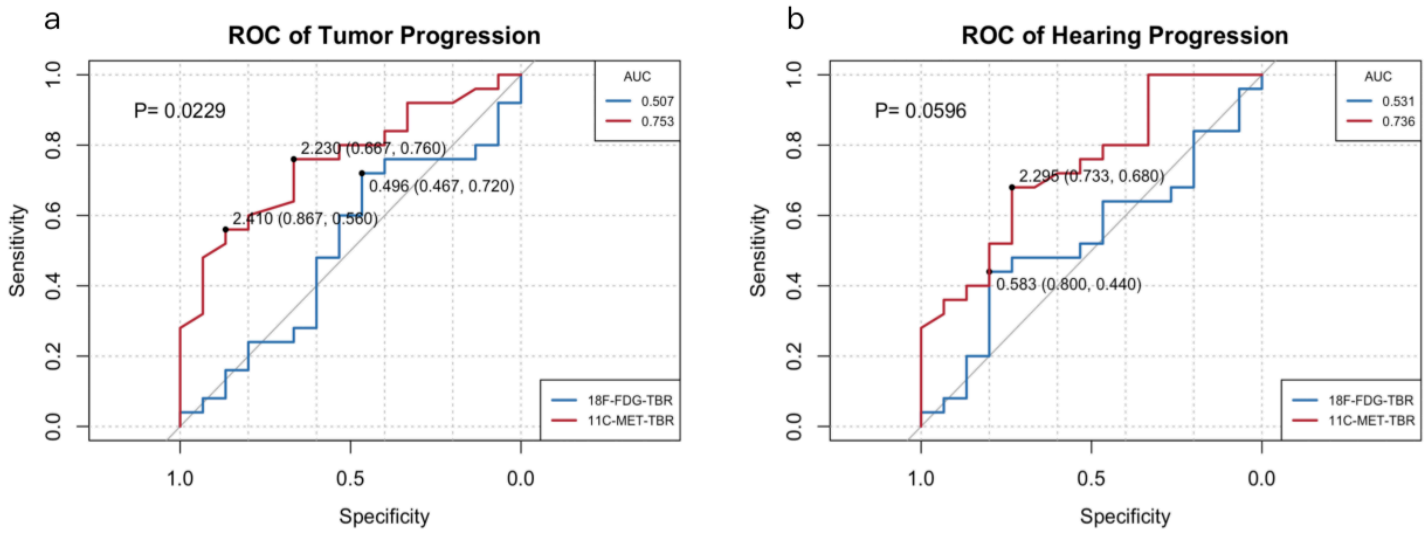


Figure 2

Receiver operating characteristic analysis of ^{11}C-methionine and ^{18}F-fluorodeoxyglucose TBRmax for predicting tumor progression and hearing deterioration. Receiver operating characteristic curves compare the predictive performance of ^{11}C-MET TBRmax (red) and ^{18}F-FDG TBRmax (blue) for (a) volumetric tumor progression and (b) hearing deterioration. For tumor progression, the AUC was 0.753 for ^{11}C-MET and 0.507 for ^{18}F-FDG (P = .0229). The selected cutoff values were 2.410 for ^{11}C-MET TBRmax and 0.496 for ^{18}F-FDG TBRmax. For hearing deterioration, the corresponding AUCs were 0.736 and 0.531, respectively (P = .0596), with cutoff values of 2.295 and 0.583. Values in parentheses beside the cutoff points indicate specificity and sensitivity, respectively. The diagonal line represents performance expected by chance. AUC, area under the curve; FDG, fluorodeoxyglucose; MET, methionine; ROC, receiver operating characteristic; TBRmax, maximum tumor-to-background ratio.

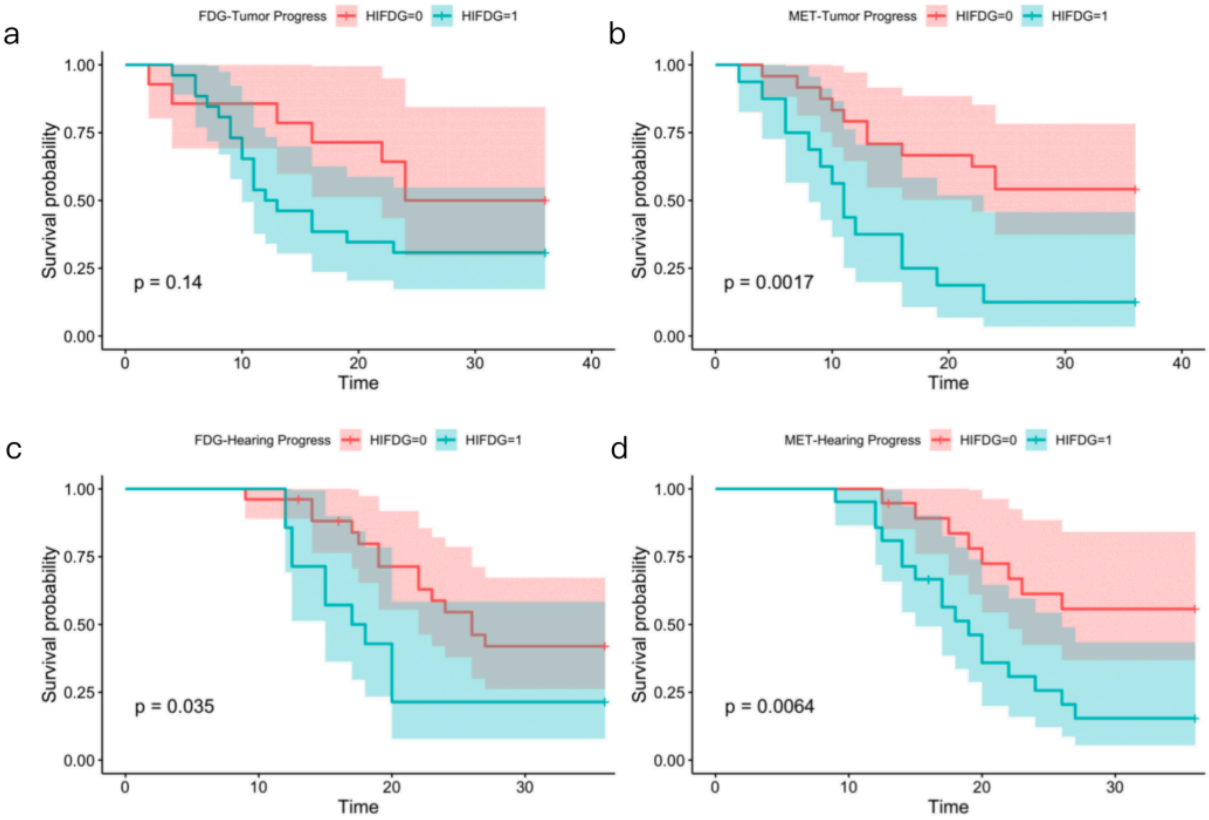


Figure 3

Kaplan–Meier analyses of tumor progression-free and hearing deterioration-free survival according to PET-derived TBRmax. Kaplan–Meier curves show (a) tumor progression-free survival stratified by ^{18}F-FDG TBRmax (cutoff, >0.496; log-rank P = .14), (b) tumor progression-free survival stratified by ^{11}C-MET TBRmax (cutoff, ≥2.410; log-rank P = .0017), (c) hearing deterioration-free survival stratified by ^{18}F-FDG TBRmax (cutoff, >0.583; log-rank P = .035), and (d) hearing deterioration-free survival stratified by ^{11}C-MET TBRmax (cutoff, ≥2.295; log-rank P = .0064). Low- and high-TBRmax groups are shown in red and turquoise, respectively. Shaded areas represent 95% confidence intervals, and tick marks indicate censored observations. Time is expressed in months. FDG, fluorodeoxyglucose; MET, methionine; PET, positron emission tomography; TBRmax, maximum tumor-to-background ratio.