

# Predictive Value of VIBE using Subtraction to Evaluate Idiopathic Facial Palsy after Starting Therapy

## Prognostischer Wert von VIBE-Subtraktionen nach Therapiebeginn bei idiopathischer Fazialisparese

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### ZUSAMMENFASSUNG

**Ziel** Prognostische Aussagekraft der 3D-VIBE-Subtraktionen (Spoiled Gradientenecho Volumetric Interpolated Breath-Hold-Examination) zur Bestimmung des Therapie-Kurzzeiteffektes bei Patienten mit Gesichtslähmung.

**Material und Methoden** Eingeschlossen wurden 97 Patienten mit idiopathischer Gesichtslähmung (52 Männer, 45 Frauen; Alter  $50,7 \pm 19,4$  Jahre), bei denen ein MRT mit Kontrastmittel nach Therapiebeginn durchgeführt wurde. Das mittlere Intervall zwischen Erkrankung und Beginn der Therapie betrug  $1,55 \pm 1,69$  Tage, zwischen Therapie und MRT-Bildgebung betrug das Intervall  $3,19 \pm 2,78$  Tage und zwischen MRT-Bildgebung und der Bewertung der therapeutischen Wirkung  $3,50 \pm 0,71$  Tage. Der Grad des therapeutischen Effekts

wurde mittels einer 4-Punkte-Skala, basierend auf der House-Brackmann-Skala für die Einstufung der Gesichtsnervenfunktion, bestimmt. 2 Radiologen werteten die Subtraktionen aus der VIBE-Sequenz (vor und nach KM-Gabe) unter Verwendung der 4-Punkte-Skala aus. Wir beurteilten die diagnostische Aussagekraft und verglichen den Grad des therapeutischen Effekts sowie die Anreicherung der Fazialisnerven, welche in 5 Segmenten bilateral eingeteilt wurde.

**Ergebnisse** Wir fanden 98 Fazialispareesen vor und eine signifikante Anreicherung in 55 nach Therapiebeginn sowie eine Restlähmung in 87 Fazialisnerven. Die Sensitivität für die Gesichtslähmung betrug 62,0%, die Spezifität 90,9%, der positive prädiktive Wert 98,2%, der negative prädiktive Wert 23,3% und die Genauigkeit 65,3%. 11 Patienten hatten eine komplette Remission, 1 Patient zeigte ein signifikantes Enhancement und die verbliebenen 10 Patienten zeigten keine signifikante Anreicherung des Fazialisnerven.

**Schlussfolgerung** VIBE hat das Potenzial, das therapeutische Ergebnis prognostisch einzuschätzen und den Grad der Gesichtslähmung nach Therapiebeginn zu beurteilen.

### Kernaussagen:

- Subtraktionen aus 3D-VIBE (Spoiled Gradientenecho Volumetric Interpolated Breath-Hold Examination) können für die Prognose bei idiopathischer Fazialisparese nach Therapiebeginn verwendet werden.
- Eine kräftige Anreicherung der Fazialisnerven in Subtraktionen aus VIBE-Sequenzen war mit einer unvollständigen Rückbildung der Fazialisparese assoziiert.
- Patienten mit gutem klinischem Verlauf zeigen kein starkes Enhancement.

### ABSTRACT

**Purpose** To determine the predictive value of 3-dimensional spoiled gradient-echo volumetric interpolated breath-hold examination (VIBE) using subtraction to evaluate the short-term effect of therapy for facial palsy.

**Materials and Methods** We included 97 patients with idiopathic facial palsy (52 male, 45 female; aged  $50.7 \pm 19.4$  years) who underwent MR imaging with a contrast agent after starting therapy. The mean interval between onset and therapy was  $1.55 \pm 1.69$  days, between therapy and MR imaging was  $3.19 \pm 2.78$  days, and between MR imaging and assessment

of the therapeutic effect was  $3.50 \pm 0.71$  days. The degree of therapeutic effect was determined using a 4-grade scale based on the House–Brackmann scale for grading facial nerve function. Two radiologists reviewed VIBE with pre- and post-contrast subtraction using the 4-point scale. We evaluated the diagnostic performance and compared the degree of therapeutic effect and enhancement of facial nerves that were divided into 5 segments bilaterally.

**Results** We identified 98 facial palsy initially and significant enhancement in 55 facial nerves after the start of therapy and residual palsy in 87. Sensitivity for all facial palsy was 62.0%, specificity was 90.9%, positive predictive value was 98.2%, negative predictive value was 23.3%, and accuracy was 65.3%. Eleven patients recovered completely, 1 showed significant enhancement, and the remaining 10 did not show significant enhancement of the facial nerve.

**Conclusion** VIBE has a potential to predict the prognostic outcome and assess facial palsy after the start of therapy.

#### Key points:

- Three-dimensional spoiled gradient-echo volumetric interpolated breath-hold examination (VIBE) using subtraction can be useful to predict residual facial palsy after initial therapy.
- Strong enhancement of the facial nerve on VIBE using subtraction was associated with residual facial palsy after the start of therapy.
- Patients with a favorable prognosis did not show strong enhancement.

#### Citation Format

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## Introduction

Facial palsy is the most common disorder of facial nerve disease and is caused by various conditions such as idiopathy, infection, trauma, and tumors. The symptoms lead to functional and cosmetic problems. It is diagnosed comprehensively by clinical findings, electrophysiological testing, and magnetic resonance (MR) imaging. Contrast-enhanced MR imaging is the most useful technique for providing diagnostic information in acute facial palsy and for excluding infarction or tumor [1, 2]. With the development of MR imaging, facial palsy has been evaluated using three-dimensional (3D) MR imaging that offers thinner slices without gaps [2–4]. T1-weighted 3D spoiled gradient-echo volumetric interpolated breath-hold examination (VIBE) is a 3D technique used to reduce motion artifacts and to improve spatial resolution, and was originally used to evaluate the abdomen before being applied to other fields [5, 6]. Subtraction between pre- and postcontrast fat-saturated VIBE is implemented because of these features.

Facial palsy should be treated as early as possible because the longer the symptoms last, the poorer the prognosis [7]. The first step in treating acute facial palsy is therapy including hydrocortisone, antibiotics, and antiviral agents. If there is no response to therapy, surgical decompression is considered depending on the symptoms and patient consent. Predicting the response to therapy for facial palsy is a challenge. Although the prognostic values of electroneurography, House–Brackmann score, and MR imaging before therapy have been reported, their usefulness remains controversial [8–10]. Moreover, electroneurography and MR imaging are time-consuming and schedules would frequently need to be adjusted after the start of therapy in clinical practice. Therefore, other methods to predict the outcome of facial palsy are required. No previous study has evaluated prognostic outcomes using MR imaging of facial palsy after starting therapy. The present study aimed to clarify whether contrast-enhanced VIBE using subtraction is useful for predicting residual facial palsy after therapy.

## Materials and Methods

Written informed consent for contrast-enhanced MRI was obtained from each patient. The study was approved by the institutional review board (Paracelsus Medical University, Nuernberg).

### Patients

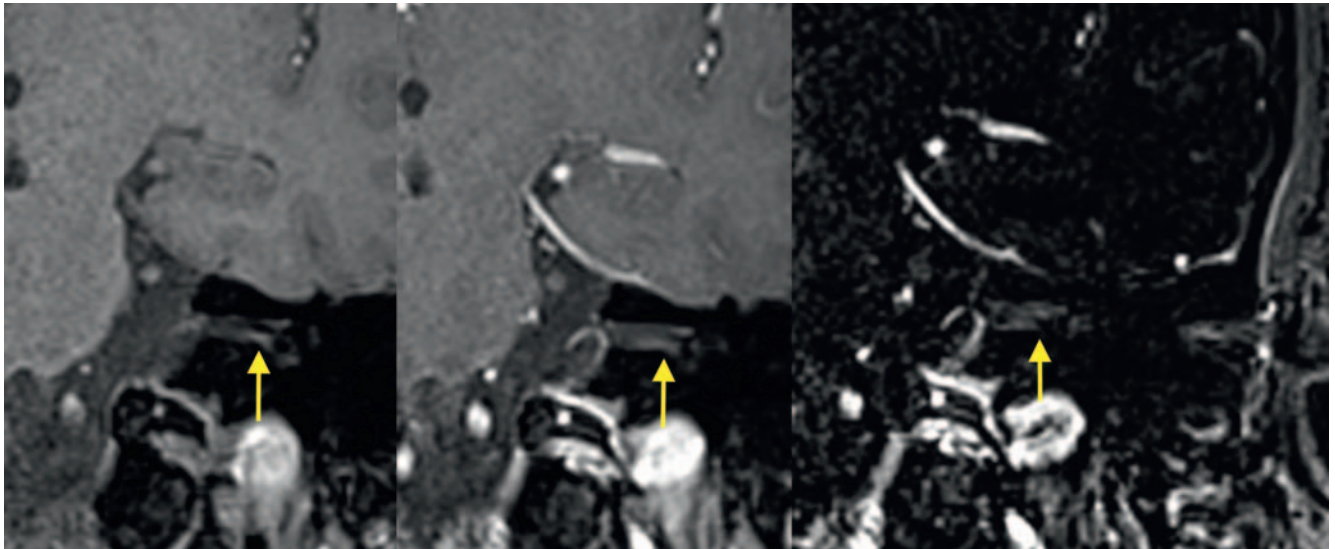
We assessed the records of 159 consecutive patients who were diagnosed with facial palsy by a neurologist or otolaryngologist and underwent contrast-enhanced VIBE from January 2013 to September 2017. We excluded 62 of these patients as follows: 1) facial palsy caused by infection including 11 Ramsay-Hunt syndrome and 5 as Lyme disease ( $n = 16$ ); 2) recurrence of facial palsy ( $n = 6$ ); 3) facial palsy with facial nerve tumor or parotid tumor ( $n = 7$ ); 4) brain metastasis or brainstem infarction ( $n = 2$ ); 5) facial palsy after head injury, operation, or radiotherapy ( $n = 5$ ); 6) no treatment for facial palsy ( $n = 5$ ); 7) lack of facial palsy grading in patient file ( $n = 7$ ); 8) one patient died; 9) two motion artifacts on contrast-enhanced MR images as judged by two radiologists ( $n = 2$ ); 10) no coronal images or subtraction obtained ( $n = 11$ ). We included 97 patients who were diagnosed as having idiopathic facial palsy in the present study (52 male, 45 female; mean age  $\pm$  standard deviation:  $50.7 \pm 19.4$  years). All patients received agents for facial palsy by infusion; 95 were treated with hydrocortisone, 1 with hydrocortisone and antiviral medication, and 1 with hydrocortisone, antibiotics, and antiviral medication.

All MR imaging was performed after starting therapy. All patients were assessed to determine the effect of therapy. The mean interval between onset of facial palsy and therapy was  $1.55 \pm 1.69$  days, between therapy and MR imaging was  $3.19 \pm 2.78$  days, and between MR imaging and assessment of therapeutic effect was  $3.50 \pm 0.71$  days.

► **Table 1** VIBE parameters on 1.5 T and 3 T imaging.

► **Tab. 1** VIBE-Parameter bei 1,5 T und 3T-MRT.

TR (ms)	TE (ms)	flip angle (degree)	thickness (mm)	bandwidth (Hz/pixel)	matrix size	field of view (cm)
10.9	3.3	14.9	1	150	256 × 230	260
20	3.7	12	1	225	320 × 272	260



► **Fig. 1** Enhancement of the left intra-auditory canal (IAC) segment is unclear on coronal postcontrast VIBE with precontrast subtraction. Left IAC segment with enhancement was detected only on subtraction, indicating a score of 1.

► **Abb. 1** Die Anreicherung des N. facialis im intrameatalen Verlauf ist in der koronaren 3D-VIBE nach KM ohne Subtraktion nicht eindeutig. Die Anreicherung im intrameatalen Segment des N. facialis wurde nur in der Subtraktion festgestellt, welche einer Skala von 1 entspricht.

## MR imaging protocols

All MR imaging from the top of the head to the bottom of the neck was obtained with a 1.5 T system (n = 61; Espree; Siemens Healthcare, Erlangen, Germany) using a 4-channel head and neck coil or a 3 T system (n = 36, Skyra; Siemens Healthcare, Erlangen, Germany) using a 20-channel head and neck coil. Coronal VIBE before and after contrast agent injection was acquired. ► **Table 1** shows the parameters of VIBE on 1.5 T and 3 T imaging. Subtraction between pre- and postcontrast VIBE was obtained. Patients received 0.1 mmol/kg of gadoteric acid (Dotarem; Guerbet, Paris, France). Contrast-enhanced VIBE was acquired within 60 s of contrast administration followed by 20 mL of saline flush.

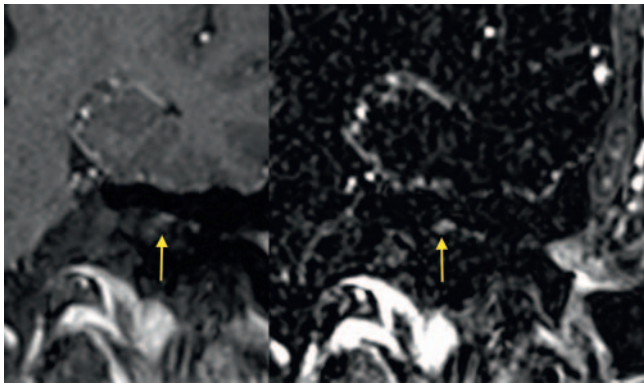
## Analysis of therapeutic effect

The House–Brackmann scale was used to characterize the degree of facial palsy [11]: with a score of normal = I; mild dysfunction = II; moderate dysfunction = III; moderately severe dysfunction = IV; severe dysfunction = V; and total palsy = VI. The degree of therapeutic effect was determined by the difference between the House–Brackmann scale score before and after treatment: no

effect = 0; mild effect = 1, but residual symptoms; moderate effect = more than 2, but residual symptoms; complete effect = disappearance of symptoms. Residual symptoms were defined as insufficient effect.

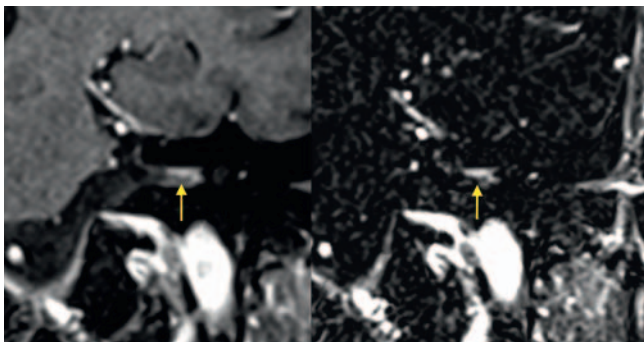
## Image analysis

Two radiologists (H.T. and K.D. with 6 and 25 years of experience, respectively in head and neck radiology) who were not involved in the clinical investigation reviewed pre- and post-contrast VIBE and subtraction, retrospectively. The observers were informed of the presence of facial palsy and the side of the lesion. However, they were blinded to other clinical information. Each facial nerve was divided into five segments: intra-auditory canal (IAC), labyrinthine, geniculate, tympanic, and mastoid segments. The observers evaluated the degree of enhancement of each segment on both sides using a 4-point scale: 0 = no enhancement; 1 = weak but definite enhancement, when the enhancement was recognized only on subtraction; 2 = moderate, less than the intensity of vascular enhancement; 3 = strong, similar to the intensity of vascular enhancement (► **Fig. 1–3**). When the enhancement pat-



► **Fig. 2** Enhancement of the left intra-auditory canal (IAC) segment is less than the intensity of vascular enhancement on coronal post-contrast VIBE with precontrast subtraction, indicating a score of 2.

► **Abb. 2** Die Anreicherung des intrameatalen Segments des N. facialis links ist geringer als die vaskuläre Anreicherung in der koronaren VIBE-Subtraktion, entsprechend einer Skala von 2.



► **Fig. 3** Enhancement of the left intra-auditory canal (IAC) segment is similar to the intensity of vascular enhancement on coronal post-contrast VIBE with precontrast subtraction, indicating a score of 3.

► **Abb. 3** Die Anreicherung des intrameatalen Segments des N. facialis links entspricht der vaskulären Anreicherung in den koronaren VIBE-Subtraktionen, entsprechend einer Skala von 3.

terns of the facial nerve made independently in the initial assessment were different, a final decision was made by consensus. An imaging score of 2 or 3 for IAC and labyrinthine segments, and 3 for geniculate, tympanic, and mastoid segments was defined as significant enhancement. An increase in the degree of enhancement of geniculate, tympanic, and mastoid segments in normal individuals has been recognized [2, 12]. Therefore, we adopted an image score of 3 to avoid overestimating enhancement.

## Analysis

Analysis was performed on the basis of the number of facial nerves. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, F1 score, and 95 % confidence interval for idiopathic facial palsy were calculated. Receiver operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) of ROC were measured to predict

the outcome for idiopathic facial palsy on VIBE. In addition, chi-square test was performed to evaluate the association between the treatment effect and age, sex, the House-Brackmann scale, and significant enhancement on VIBE using subtraction. In accordance with the previous studies, each predictor was divided into 2 groups: age was divided into > 50 years and  $\leq$  50 years; sex was divided into male and female; the House-Brackmann scale was divided into I–IV and V or VI [13, 14]. Also, we compared the degree of therapeutic effect and enhancement of the facial nerve.

## Results

### Diagnostic performance of MR imaging to detect residual facial palsy after the start of therapy

MR images of 97 patients were all of good or excellent image quality allowing the assessment of the facial nerve up to the stylo-mastoid foramen. In 20 patients, therapy had no effect on the symptoms of facial palsy, and in 53 patients a mild and in 13 patients a moderate effect was documented. 11 patients recovered completely. There were 55 facial nerves with significant enhancement: 28 (right facial nerve), 25 (left facial nerve), and 1 (bilateral). ► **Table 2** shows the diagnostic performance of MR imaging to predict the therapeutic effect for facial nerve palsy. AUCs of the predictive values using VIBE were 0.761 for idiopathic facial palsy (► **Fig. 4**).

### Comparisons of the therapeutic effect and enhancement seen on MR imaging

► **Table 3** shows the comparisons of the therapeutic effect and the predictors. No significant differences were found between the groups of age, sex, and HB ( $p=0.719$ ,  $p=0.809$ , and  $p=0.345$ , respectively). The differences between the treatment effect and enhancement of the facial nerve were significant ( $p=0.016$ ). In patients with residual symptoms, the degree of significant enhancement was higher than that of insignificant enhancement. Conversely, the degree of significant enhancement was lower in patients who recovered from symptoms. ► **Fig. 5** shows the relationship between each segment and the degree of enhancement in all patients included. In patients with residual facial palsy, there were 55 facial nerves with significant enhancement in IAC and labyrinthine segments, and 15 for geniculate, tympanic, and mastoid segments. Although an image score of 3 was identified in patients with residual facial palsy, facial nerve with strong enhancement was not revealed when the symptoms disappeared after starting therapy.

## Discussion

In the present study, we found that a high signal intensity of the facial nerve in contrast-enhanced high-resolution T1-weighted 3D gradient echo imaging was associated with an unfavorable prognosis, including residual facial palsy in the short-term clinical follow-up after therapy. Patients with a favorable prognosis and

► **Table 2** Diagnostic performance to predict the short-term effect of therapy for facial palsy.

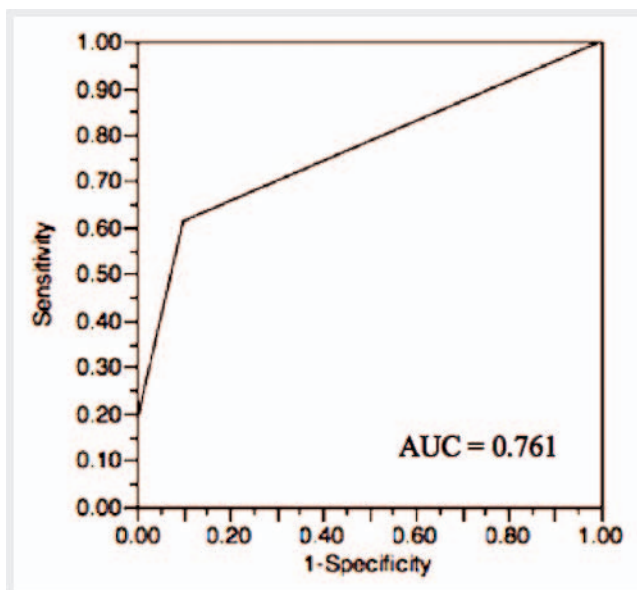
► **Tab. 2** Diagnostische Aussagekraft zur Vorhersage der kurzfristigen Wirkung der Therapie bei Gesichtslähmung.

	sensitivity [95 % CI]	specificity [95 % CI]	PPV [95 % CI]	NPV [95 % CI]	accuracy [95 % CI]	F-1 score
all (n = 98)	62.0 % [58.2–62.6]	90.9 % [64.1–98.4]	98.2 % [92.7–99.7]	23.3 % [16.4–25.2]	65.3 % [58.9–66.6]	75.7 %

► **Table 3** Comparisons between the degree of therapeutic effect and enhancement of facial nerve for all facial palsy, idiopathic facial palsy, and infectious facial palsy.

► **Tab. 3** Vergleiche zwischen dem Grad des therapeutischen Effekts und der KM-Anreicherung der Gesichtsnerven bei idiopathischer Gesichtslähmung.

for idiopathic facial palsy (n = 98)	no effect	mild effect	moderate effect	complete effect	total	p
≤ 50 years	10	30	7	7	54 (55.1 %)	0.719
> 50 years	10	24	6	4	44 (44.9 %)	
male	11	28	8	6	53 (54.1 %)	0.809
female	9	26	5	5	45 (45.9 %)	
–	15	41	11	10	77 (78.6 %)	0.345
or	5	13	2	1	21 (21.4 %)	
significant enhancement	12	33	9	1	55 (56.1 %)	0.016
insignificant enhancement	8	21	4	10	43 (43.9 %)	



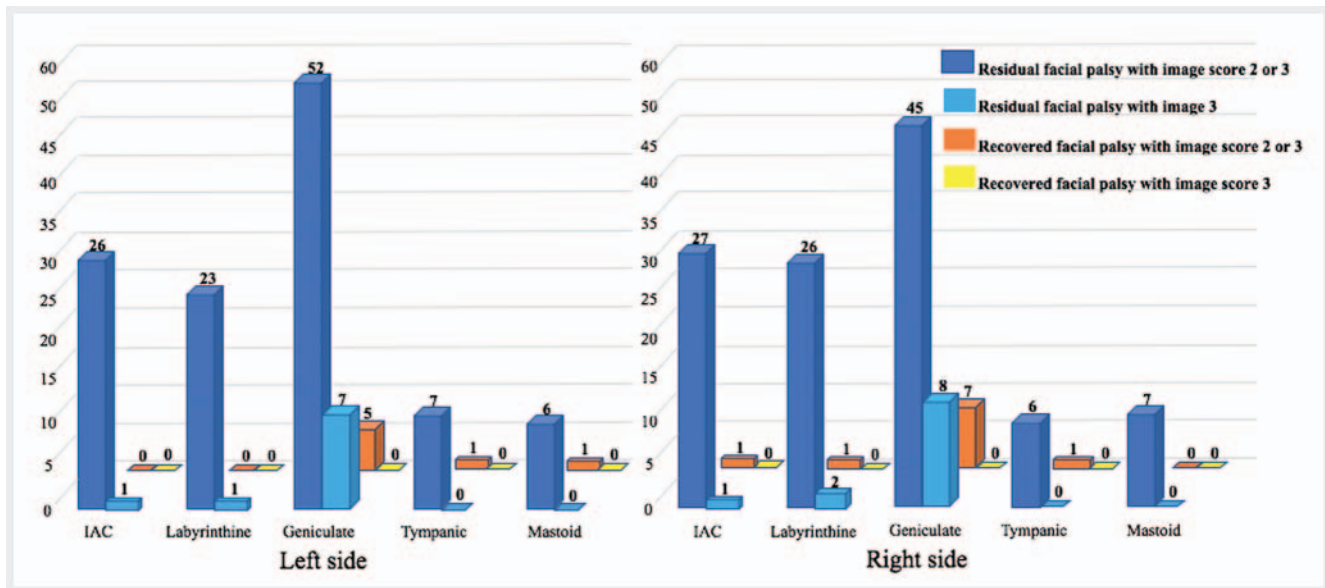
► **Fig. 4** Receiver operating characteristic (ROC) curves and the area under the curve (AUC) of ROC for predicting the outcome for idiopathic facial palsy on VIBE.

► **Abb. 4** ROC-Kurve und AUC-Kurve zur Prognoseeinschätzung des klinischen Ergebnisses der idiopathischen Fazialisparese aus den VIBE-Subtraktionen.

disappearance of the symptoms after therapy did not show strong enhancement of the facial nerve.

MR imaging to predict the outcome of facial palsy has produced controversial findings. While some authors concluded that MR imaging might not predict the outcome with sufficient reliability [7, 15], others concluded that MR imaging had the potential to predict poor outcome [16, 17]. Kress et al. showed that patients with contrast enhancement of the nerve within the IAC had a poor outcome. The outcome was correlated with electro-neurography performed 7 days after disease onset [16]. However, to our knowledge, no previous studies have reported the prognostic ability of MR imaging for facial palsy after starting therapy.

Contrast-enhanced facial nerves seen on T1-weighted turbo spin-echo (TSE) sequences have identified idiopathic and infectious facial palsy, which is explained by disruption of the blood-peripheral nerve barrier and venous congestion in the perineural space [2, 12, 17]. Lim et al. have suggested the usefulness of high-resolution contrast-enhanced 3D T1-fast-field echo and 3D fluid attenuation inversion recovery (FLAIR) to assess facial palsy [4]. Yun et al. found that the diagnostic performance of 3D isotropic T2-weighted fast spin-echo (VISTA) was superior to T1-TSE [3]. Because the signal intensity of the facial nerve on nonenhanced T1-weighted 3D gradient echo imaging could be intermediate or slightly elevated due to flow-related enhancement [18], we used pre- and postcontrast subtraction VIBE, which can mitigate motion artifacts for short acquisition times, avoiding pseudo-enhancement of the facial nerve.



► **Fig. 5** Comparisons between each segment and the degree of enhancement in all patients with residual or recovered facial palsy.

► **Abb. 5** Vergleiche zwischen den Segmenten des N. facialis und dem Anreicherungsgrad bei allen Patienten mit residueller oder vollständiger Rückbildung.

Of note is that the normal facial nerve can show contrast enhancement on MR imaging in up to 76% of cases because of the venous plexus along the facial nerve, especially in the geniculate, tympanic, and mastoid segments [2, 19]. In our present study, we averaged 2 proximal segments (IAC and labyrinthine) and 3 distal segments of the facial nerve (geniculate, tympanic, and mastoid). In patients who recovered from facial palsy, an image score of 2 for geniculate, tympanic, and mastoid segments was confirmed, and there was no image score of 3 for those segments. Strong enhancement of the facial nerve after starting therapy was associated with residual facial palsy. The PPV of contrast enhancement of the facial nerve was 98.2%.

The specificity of contrast enhancement for residual facial palsy was 90.9%. The enhancement of facial nerves in patients who recovered from facial palsy was decreased, and this may have resulted from the improvement of inflammatory and edematous changes. At the same time, the sensitivity was 62.0%, while Lee et al. described that contrast-enhanced 3D MR imaging had an advantage for evaluating facial neuritis. The sensitivity was 100% for contrast-enhanced 3D T1-fast field echo and 97.2% for contrast-enhanced 3D FLAIR in 36 patients with facial neuritis [4]. Although patients without enhancement had a more favorable prognosis, there were patients with residual facial nerve palsy after starting treatment without enhancement. The lack of enhancement might be attributed to a suppression of inflammation.

The present study has several limitations. First, the two radiologists evaluated the degree of enhancement of facial nerve visually. Second, both 1.5T and 3T MR imaging were adapted. Third, the interval between onset, initiation of treatment, and the MR examination varied. Especially the interval between MR and

assessment of therapeutic effect was short. Peitersen described that 71% of patients with Bell's palsy recovered completely by 6 months and all patients with Bell's palsy showed some improvement [20, 21]. Therefore, the extended follow-up in this study may have provided additional information for the outcomes. Further longitudinal cohort studies are needed to compare MR imaging findings with symptoms after long-term follow-up.

## Conclusion

VIBE using pre- and postcontrast subtraction has potential to predict residual facial palsy and assess the short-term effect of therapy. Further investigation with long-term follow-up will be required to validate our results.

### CLINICAL RELEVANCE OF THE STUDY

- VIBE using subtraction provides the noninvasive method to predict residual facial palsy after the start of therapy.
- Strong enhancement of the facial nerve on VIBE using subtraction can be associated with residual facial palsy.
- The degree of enhancement can be higher in patients with residual symptoms compared with recovered patients.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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