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**Zusammenfassung des wissenschaftlichen Inhalts**

**(Arno Olthoff)**

In Deutschland sind 12% der über 60-Jährigen von einer Schluckstörung („Dysphagie“) betroffen. Nach einem Schlaganfall leiden bis zu 30% und bei neurodegenerativen Erkrankungen bis zu 80% der Patienten an einer Dysphagie. Bei Aspirationsneigung ist diese lebensbedrohlich und der bildgebenden Dysphagie-Diagnostik kommt eine entscheidende Bedeutung in der Erkennung, Klassifizierung und Therapieplanung zu. Den klinisch etablierten Methoden der flexibel-endoskopischen Evaluation des Schluckens (FEES) und radiologischen Videofluoroskopie (VF) sind hierbei technische Grenzen bezüglich der Abbildung und Analyse gesetzt. Als aussichtsreich erwies sich in Vorstudien an gesunden Probanden die Abbildung des Schluckvorganges im neu entwickelten Echtzeit-MRT.

Patienten mit einer Einschlusskörpermyositis (*inclusion body myositis*, IBM) weisen durch ihre Muskelerkrankung oft eine erhebliche Schluckstörung auf, die durch das Aspirationssrisiko als Hauptfaktor für die erhöhte Sterblichkeit der Erkrankung gilt. Die Schluckstörung der IBM ist durch verschiedene Arbeiten von uns und anderen Arbeitsgruppen bereits gut charakterisiert worden: Durch eine funktionelle Enge des oberen Ösophagusphinkters kommt es zu Einschluckstörungen. In der vorliegenden Arbeit wurde der Nutzen der Echtzeit-MRT für die klinische Diagnostik geprüft. Die Echtzeit-MRT erwies sich im Vergleich zur FEES und zur VF als gleichwertig in Bezug auf die Detektion und Graduierung einer Dysphagie. Zudem ermöglichte die MRT die Vermessung von Weichteilbefunden und zeitlichen Abläufen von Ereignissen. Der unmittelbare Nutzen ist vor allem auch die Vermeidung von Röntgenstrahlung bei gleicher diagnostischer Sicherheit. Dadurch wird insbesondere ermöglicht, dass Patienten zur Therapiekontrolle und in klinischen Studien im Verlauf untersucht werden können. Darüber hinaus lassen die neuen Möglichkeiten der Weichteildarstellung und –analyse im MRT einen inhaltlichen Zugewinn in der Dysphagie-Diagnostik erwarten. Der unmittelbare klinische Nutzen der Echtzeit-MRT wird derzeit bei weiteren Dysphagie-Patienten mit anderen neurologischen und strukturellen Erkrankungen des Schlucktraktes geprüft.

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# Evaluation of dysphagia by novel real-time MRI



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## ABSTRACT

**Objective:** To assess safety and feasibility of real-time (RT) MRI for evaluation of dysphagia and to compare this technique to standard assessment by flexible endoscopic evaluation of swallowing (FEES) and videofluoroscopy (VF) in a cohort of patients with inclusion body myositis (IBM).

**Methods:** Using RT-MRI, FEES, and VF, an unselected cohort of 20 patients with IBM was studied as index disease with a uniform dysphagia. Symptoms of IBM and dysphagia were explored by standardized tools including Swallowing-Related Quality of Life Questionnaire (SWAL-QoL), IBM Functional Rating Scale, Patient-Reported Functional Assessment, and Medical Research Council Scale.

**Results:** Dysphagia was noted in 80% of the patients and SWAL-QoL was impaired in patients with IBM compared to published reference values of healthy elderly. Swallowing in a supine position during RT-MRI was well-tolerated by all patients. RT-MRI equally revealed dysphagia compared to VF and FEES and correlated well with the SWAL-QoL. Only RT-MRI allowed precise time measurements and identification of the respective tissue morphology. The pharyngeal transit times were 2-fold longer compared to published reference values and significantly correlated with morphologic abnormalities.

**Conclusions:** RT-MRI is safe and equally capable as VF to identify the cause of dysphagia in IBM. Advantages of RT-MRI include visualization of soft tissue, more reliable timing analysis, and lack of X-ray exposure. RT-MRI may become a routine diagnostic tool for detailed assessment of the esophagus and other moving parts of the body, facilitating longitudinal evaluations in daily practice and clinical trials. *Neurology*® 2016;87:1-7

## GLOSSARY

**CI** = confidence interval; **CP** = cricopharyngeal propulsion; **EOT** = esophageal opening time; **FEES** = flexible endoscopic evaluations of swallowing; **IBM** = inclusion body myositis; **IBM-FRS** = IBM Functional Rating Scale; **MRC** = Medical Research Council; **OTT** = oral transfer time; **PTT** = pharyngeal transfer time; **ROI** = region of interest; **RT-MRI** = real-time MRI; **SWAL-QoL** = Swallowing-Related Quality of Life; **UES** = upper esophageal sphincter; **VF** = videofluoroscopy.

Dysphagia is common in neurodegenerative disorders (e.g., Parkinson disease), myopathies, and stroke, and is associated with a reduced quality of life and life-threatening complications (e.g., aspiration pneumonia).<sup>1,2</sup> Yet diagnostic tools for evaluating dysphagia are not fully developed and despite significant radiation exposure, videofluoroscopy (VF) has remained the gold standard in swallowing diagnostics for almost 2 decades.<sup>3</sup> The addition of flexible endoscopic evaluations of swallowing (FEES) could not replace VF.<sup>4</sup> Both are used for descriptive analyses and the Rosenbek penetration-aspiration scale is mainly used to classify the degree of dysphagia.<sup>5</sup> Quantitative measures have methodical restrictions of FEES and VF. A reliable method that can be repeated without X-ray exposure and the possibility to visualize the soft tissue is highly desirable in daily routine as well as for clinical studies.

Preceding studies of healthy individuals demonstrated that a novel method of real-time MRI (RT-MRI) was suitable to display the course of swallowing.<sup>6,7</sup> In the present study, we assessed

Supplemental data  
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the safety and feasibility of this novel RT-MRI as a diagnostic tool in patients with dysphagia. RT-MRI was compared to VF and FEES with regard to morphologic and functional findings.

As index disease with dysphagia, we studied an unselected cohort of patients with inclusion body myositis (IBM) as they often have dysphagia.<sup>8–11</sup>

**METHODS** **Participants.** Twenty consecutive patients were recruited from the local Department of Neurology between 2012 and 2014. Diagnosis of IBM was based upon the most recent European Neuromuscular Centre criteria.<sup>12</sup> Absence of severe aspiration was confirmed by medical history and FEES examination per Langmore criteria.<sup>4</sup> Data collection was scheduled for one visit.

**Standard protocol approvals, registrations, and patient consents.** The study was in accord with good clinical practice and approved by the local ethics committee and all participants gave written informed consent prior to examination.

**Questionnaires and clinical examination.** To assess the influence of dysphagia on quality of life, we used the Swallowing-Related Quality of Life (SWAL-QoL) questionnaire. This patient-based questionnaire ranges from 100 points (normal swallowing) to 0 points (major dysphagia). The SWAL-QoL is validated<sup>13</sup> and was used for assessing dysphagia in amyotrophic lateral sclerosis and Parkinson disease.<sup>14,15</sup> The IBM Functional Rating Scale (IBM-FRS) and the Patient-Reported Functional Assessment for patients with IBM were used to assess function. Muscle strength was evaluated by Medical Research Council (MRC) scale (0 to 5) and included head flexion/extension, arm abduction, elbow flexion/extension, wrist flexion/extension, finger flexion/extension, hip flexion/extension, knee flexion/extension, and ankle flexion/extension. Rating of both sides led to a maximum MRC sumscore of 140.

**Imaging techniques. Flexible endoscopic evaluation of swallowing.** Transnasal FEES was performed in a sitting position and videorecorded with a typical temporal resolution of 25 frames per second (fps). An oral bolus of 1 teaspoon (5 milliliters) green pear pie was used to ensure a clear contrast to the tissues of the oropharyngeal tract. The flexible endoscope (Olympus ENF, Hamburg, Germany) was connected to a camera (Olympus visera OTV-S7) and all videos (videos 1–6 at Neurology.org) were stored on a hard disk (rpSzene; Rehder & Partner GmbH, Hamburg, Germany) for subsequent evaluation.

**Videofluoroscopy.** VF was performed in a sidewise standing position with a resolution of 3–8 fps using either Axiom Sirekop SD (Siemens, Eschborn, Germany) or Panthoskop P5 (Siemens). Clear contrast of oropharyngeal tissue was obtained with an oral bolus of about 20 milliliters liquid contrast agent (either Imeron 350 or GastroLux). Recorded videos were stored in a PACS system (Centricity PACS 3.2; GE Healthcare, Barrington, IL).

**RT-MRI.** Dynamic MRI of swallowing was performed on a 3T clinical MRI system (Tim Trio, Siemens Healthcare, Erlangen, Germany) using the previously established RT-MRI technique,<sup>16,17</sup> based on a highly undersampled radial fast low-angle shot acquisition in combination with image reconstruction by regularized nonlinear inversion.<sup>18</sup> A bolus of 5 mL pineapple juice, thickened with yeast (Quick & Dick, Pflimmer Nutrica, Erlangen, Germany),

was used as oral contrast agent due to its natural content of paramagnetic manganese, which leads to a bright signal in T1-weighted images.<sup>6,7</sup> The grade of viscosity was adjusted to an equal level as the liquid contrast agents used for FEES and VF.

Participants were examined in a supine position with a combination of a small flexible coil (Siemens Healthcare) covering the lower face and a bilateral 2 × 4 array coil (NORAS MRI Products, Hoechst, Germany) centered to the thyroid prominence on both sides of the neck. Successive T1-weighted images (repetition time 2.17 milliseconds, echo time 1.44 milliseconds, flip angle 5°, field of view 192 × 192 mm<sup>2</sup>) were acquired with an in-plane resolution of 1.5 × 1.5 mm<sup>2</sup> and a slice thickness of 10 mm in a mid-sagittal plane. The total image acquisition time was 41.23 milliseconds, which yielded a true temporal resolution of 24.3 fps. Further details were presented before.<sup>6,16–18</sup> Conventional high-resolution T2-weighted MRI of the upper esophageal sphincter was performed in a sagittal orientation.

**Image analysis. Clinical function and morphology.** VF, FEES, and RT-MRI results were evaluated according to (1) the oral control of the bolus, (2) bolus transport, (3) velo-pharyngeal closure, (4) retentions of the bolus in the pharyngeal tract, (5) laryngeal penetration, and (6) aspiration, which were all arbitrarily graded on a 4-point-scale (3 = normal, 0 = severe pathology). Evaluations of all methods were performed by 2 independent specialists, who were masked for each other's score and all results of other methods. The mean of both scorings was used for subsequent analysis.

**Quantitation of swallowing events.** For quantitative evaluation, the viewing software OsiriX MD (open-source software: osirix-viewer.com) was used. Start and end points of distinct deglutition events were analyzed frame by frame in the most relevant sagittal view.<sup>6,7</sup> For relative timings, the oro-velar opening (velum elevation from dorsum of tongue) was chosen as start time.<sup>7</sup> Measures focused on oral transfer time (OTT; from start to oro-velar closure), pharyngeal transfer time (PTT; bolus passage from pharynx to esophagus), and esophageal opening time (EOT; from opening until closure of the upper esophageal sphincter [UES]). Laryngeal elevation and the extent of the morphologic finding of the UES were measured in millimeters per region of interest (ROI) tool from OsiriX MD. All timings were assessed in consensus by 2 masked specialists.

**Statistical analyses.** Bland-Altman plots (including 95% limits of agreement) were used to investigate the agreement among the 3 techniques, i.e., FEES, VF, and RT-MRI.<sup>19</sup> The interrater agreement was assessed by the Krippendorff  $\alpha$  coefficient.<sup>20</sup> Associations between variables were assessed by Pearson correlation coefficients. Comparison between 2 groups was made by *t* test. Statistical analyses were performed using the software GraphPad Prism 6 (San Diego, CA) and SAS version 9.4 (Cary, NC). Due to the exploratory nature of this investigation, *p* values were not adjusted for multiple testing and *p* values  $\leq 0.05$  were considered significant.

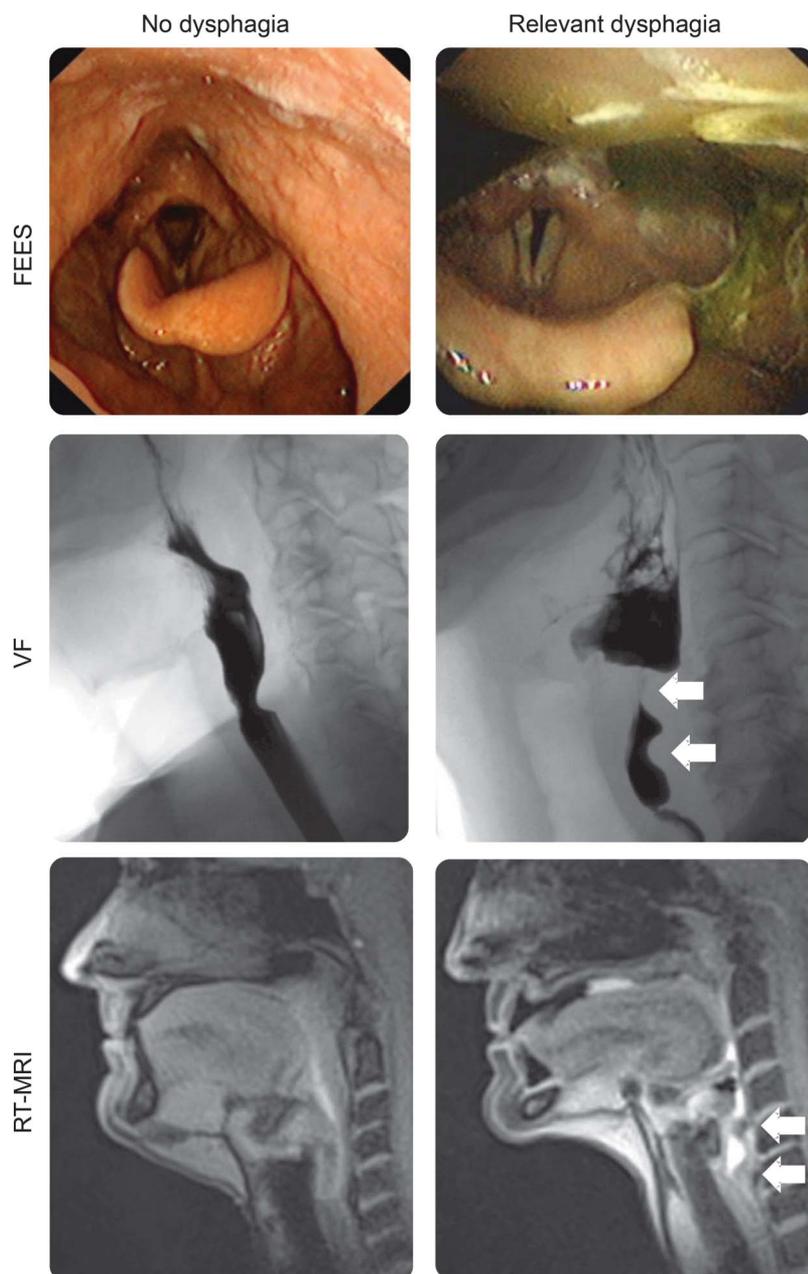
## RESULTS Characterization of the patient cohort.

Twenty-two unselected patients with IBM were included in this study and 2 patients were subsequently excluded: one could not be lifted onto the MRI table; another patient died from a ruptured aortic aneurysm before the planned assessments. The results of all 20 participants were used for analysis (overview of all raw data in table e-1). Twelve participants were men (60%); the mean age ( $\pm$ SD) was 72  $\pm$  7 years.

SWAL-QoL revealed a broad range of the severity of dysphagia within the patient cohort and the scores were pathologic compared to previously validated values in aged individuals without dysphagia.<sup>15,21</sup> Eighty percent of the patients displayed symptoms of dysphagia. A correlation between restrictions in daily life activities (IBM-FRS), muscle strength (MRC scale), and the patient-reported measure of swallowing

(SWAL-QoL) were observed (figure e-1: MRC vs IBM-FRS:  $r = 0.83$ , 95% confidence interval [CI] 0.61–0.93,  $p = 0.0001$ ; SWAL-QoL vs IBM-FRS:  $r = 0.6$ , 95% CI 0.22–0.82,  $p = 0.0051$ ). No statistically significant correlation was noted between positivity for the Mup44 autoantibody (9 out of 20 patients were positive, table e-1) and any patient-reported outcome scale or results of the technical assessments (not shown).

**Figure 1** Representative swallowing imaging: Endoscopy, videofluoroscopy, and real-time MRI



Exemplary findings of swallowing in patients with inclusion body myositis without and with relevant dysphagia by real-time MRI (RT-MRI), videofluoroscopy (VF), and flexible endoscopic evaluation of swallowing (FEES). The white arrows indicate the cricopharyngeal propulsion as noted by VF and RT-MRI. RT-MRI and VF show the moment of the passage of the bolus through the upper esophageal sphincter while the FEES show the top view on the larynx and the recessus piriformis after passage of the bolus.

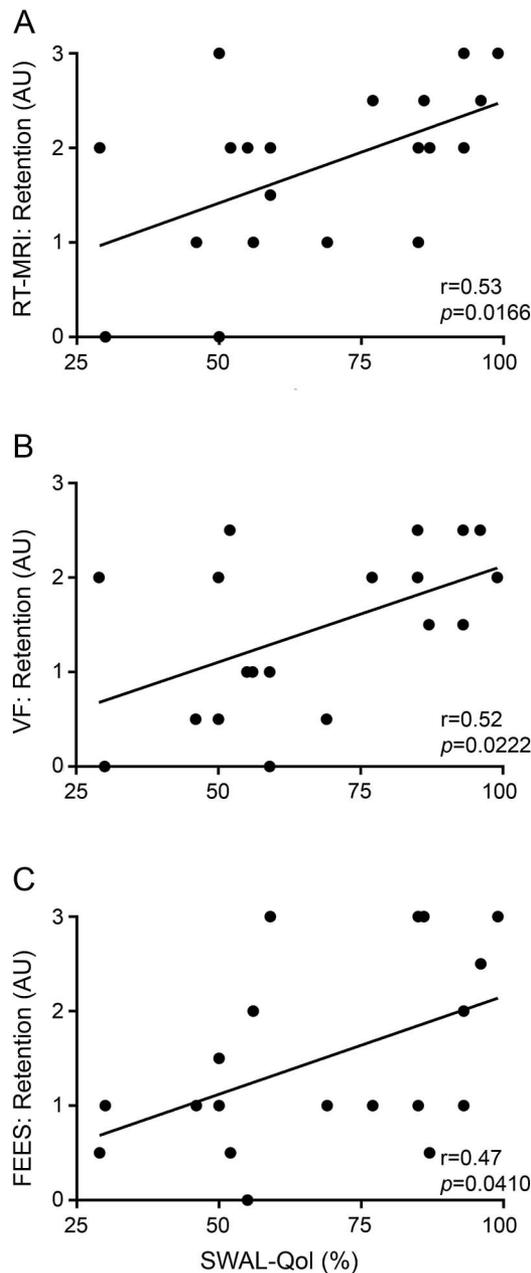
**Assessment of swallowing by FEES, VF, and RT-MRI.** A cricopharyngeal propulsion (CP) in the region of the UES was identified during swallowing by VF and RT-MRI, but not by FEES (figure 1). In VF, the CP appeared similar to a cricopharyngeal bar that can be observed, e.g., in the Zenker diverticulum, which was not observed in our cohort. At rest, T2-weighted MRI revealed no morphologic abnormalities or CP within the esophagus, which excluded other causes for dysphagia, such as a tumor.

Relevant parameters of swallowing included bolus control and transport, velo-pharyngeal closure, laryngeal penetration, aspiration, and bolus retention in the pharyngeal tract. The latter is believed to be the most sensitive indicator of functional deficits in swallowing and was reliably identified by all 3 modalities (FEES, VF, RT-MRI). This parameter was scored by 2 independent investigators using a 4-point scale (figure 2A). Bland-Altman plots did not reveal any systematic deviation between these methods (figure 2B). Penetration was seen in 2 patients (10%) by RT-MRI and in 6 patients (30%) by FEES or VF. Aspiration was suspected by one rater in one patient by FEES and RT-MRI and in 3 patients by VF. The interrater agreement was assessed for bolus transport and retention. The Krippendorff  $\alpha$  was 0.39 (RT-MRI), 0.55 (VF), and 0.67 (FEES) for bolus transport, and 0.51 (RT-MRI), 0.52 (VF), and 0.52 (FEES) for retention. Penetration and aspiration were rare events and the scoring was mostly 3 on the aforementioned 4-point scale, rarely 2, and never 1 or 0. Since standard measures for interrater agreement including the Krippendorff  $\alpha$  are corrected for random agreement, under these conditions, a statistical paradox occurs<sup>22</sup> with the measure for agreement suggesting a low degree of agreement although the observed agreement is very high. Therefore, no formal assessment of interrater agreement is reported here for penetration and aspiration.

Aspiration was clinically unapparent and episodes were not accompanied by symptoms like coughing or dyspnea. All patients felt comfortable with swallowing in a supine position and even preferred this compared to sitting during VF. The self-assessment of patients by SWAL-QoL correlated to the grade of retention as reflected by RT-MRI, VF, and FEES (RT-MRI vs SWAL-QoL:  $r = 0.52$ , 95% CI 0.11–0.79,



**Figure 3** Correlation between swallowing assessments and subjective symptoms



Correlation between the subjective impairment of swallowing and technical examinations. The assessment of retentions by 2 different evaluators on a 4-point scale (3 = normal swallowing; 0 = severe retention; same data as in figure 2A) was correlated with the Swallowing-Related Quality of Life scale (SWAL-QoL), a well-established patient-reported outcome measure for dysphagia. A significant correlation was noted with real-time MRI (RT-MRI) (A), videofluoroscopy (VF) (B), and flexible endoscopic evaluation of swallowing (FEES) (C). Exclusion of 2 datasets was required due to technical impairment of 1 VF and 1 FEES. AU = arbitrary unit.

tissue is restricted; and (3) aberration of images impair absolute measurements. Dynamic CT images with a time resolution of 10 fps<sup>25</sup> carry the disadvantages of X-ray exposure and a restricted time resolution.

IBM serves as an ideal group of patients for a clinical application of RT-MRI as a diagnostic tool for the evaluation of swallowing since (1) patients with IBM have a typical type of dysphagia; (2) not all patients have dysphagia, which enables an ideal comparison within this cohort; (3) the disease does not impair cognition or memory, so that informed consent and cooperation are unaffected. In line with our previous study,<sup>6,7</sup> RT-MRI in a supine position was well-tolerated by all participants. The frequency of 80% of dysphagia was well in line with previous observations.<sup>8</sup> Despite a major relevance of dysphagia in IBM including associations with cachexia,<sup>8</sup> pneumonia,<sup>26</sup> and increased mortality,<sup>27</sup> dysphagia is often overlooked and may be more readily picked up by the routine use of standardized questionnaires.

For the evaluation of swallowing, an arbitrary, self-designed 4-point scale was used instead of the established Rosenbek penetration-aspiration scale.<sup>5</sup> This was necessary because patients with aspiration were excluded and retention is not assessable with the Rosenbek scale.<sup>5</sup> Retention is seen as the most sensitive marker for dysphagia even in clinically unapparent cases.<sup>28</sup> Penetration is a potential risk factor for aspiration and represents a clinical rise to severe dysphagia. The lower rate of detection of penetration by RT-MRI (10% in RT-MRI vs 30% in FEES and VF) may be due to a smaller bolus of only 5 mL in RT-MRI. In addition, due to logistical issues, the assessments could not always be performed on the same day. Third, validity of the data is impaired by the small size of the cohort. A future evaluation of a larger cohort will include the use of a 10-milliliter bolus, which, for safety reasons, was avoided in this initial study.

In contrast to VF, RT-MRI provided quantitative functional and morphologic pathologies. In VF, dimensional measurements suffered from aberration of image scales and software embedment. Due to a 1:1 image scale in RT-MRI, measures of laryngeal elevation and morphologic dimension were easily accomplished using digital ROI tools from a standard digital imaging and communications in medicine viewer. Combined with the superior illustration of soft tissues, the novel RT-MRI method was favored for structural and functional measures of morphologic structures. Functional measures referred to timings of oral, pharyngeal, and esophageal bolus transport and to the extent of laryngeal elevation and the size of the CP. Our data comparison with reference values from a former study with healthy young volunteers suffers from a significant difference of age. The preliminary result of prolonged transport timings in IBM has to be proved in groups of age-adapted samples.

Other groups have assessed the pressure profile of the oropharynx and hypopharynx and the manometry

of the UES. However, these data are inconsistent and failed to provide a reliable profile in IBM.<sup>11,29</sup> Therefore, our present study was focused on the comparison of imaging techniques. Future studies will aim to identify the clinicomorphologic dysfunction that causes dysphagia in IBM, possibly a weakness of suprahyaloidal muscles, which disturbs the precise concert of contraction of swallowing muscles and impairs the bolus transport across the UES.

Because of technical restrictions in clinical routine examination, neither VF nor FEES exceeded the evidence level of qualitative analyses and descriptive reports. Recently, ultrasonographic B-mode videos were compared to VF and FEES in order to detect dysphagia but did not reach equivalent sensitivity.<sup>30</sup> By contrast, RT-MRI provides the basis for a quantitative assessment of functional as well as structural findings during swallowing. The advantage of quantitative data in dysphagia will be, e.g., a longitudinal evaluation of therapeutic interventions.

Using VF, other groups reported a number of different assumptions about the UES morphology and its presumed impairment of contraction in IBM. An impaired laryngeal elevation and a failed relaxation of the UES were discussed as underlying mechanisms for dysphagia in IBM.<sup>8,10,11,29,31</sup> Our present study confirms that CP is a major morphologic abnormality in IBM and could also be interpreted as functional achalasia of the UES. Accordingly, a significant correlation to the duration of the PTT was demonstrated. However, our present RT-MRI and VF analysis of laryngeal elevation did not reveal any major abnormalities. Moreover, there was no significant correlation between laryngeal elevation and the degree of dysphagia or the extent of the CP. In contrast to previous observations by others, an impaired laryngeal elevation was not observed in our study. This may be explained by the nature of our IBM cohort and exclusion of patients with severe dysphagia and history of aspiration. We noted a systematic deviation with higher values for the laryngeal elevation in RT-MRI compared to VF in Bland-Altman analysis. Bearing in mind the possible bias of a small cohort (n = 14) that encompassed quantifiable data of laryngeal elevation per 2 different methods (RT-MRI and VF), this finding might suggest that different forces of gravity in different body positions could affect swallowing to some degree.

RT-MRI was demonstrated to be noninferior compared to the standard assessments VF and FEES. Assessment in a supine position did not cause disadvantages or unwanted events. It is expected that RT-MRI will develop as a useful diagnostic tool for assessment of dysphagia in various conditions. Further studies with RT-MRI are planned to determine the causes and degrees of dysphagia in other myopathies and other neurologic and non-neurologic disorders that impair swallowing.

## AUTHOR CONTRIBUTIONS

Arno Olthoff designed the study, supervised the study, acquired and analyzed the data, interpreted the data, drafted the manuscript, and revised the manuscript. Per-Ole Carstens acquired and analyzed the data, interpreted the data, drafted the manuscript, and revised the manuscript. Shuo Zhang acquired and analyzed the data. Eva von Fintel acquired and analyzed the data. Tim Friede revised the manuscript and conceived and assisted with the statistical analyses. Joachim Lotz supervised the study, interpreted the data, and revised the manuscript. Jens Frahm designed and supervised the study. Jens Schmidt designed and supervised the study, interpreted the data, and revised the manuscript.

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## DISCLOSURE

A. Olthoff reports no disclosures relevant to the manuscript. P.-O. Carstens has received reimbursements for travel from Allergan, CSL Behring, Grifols, and Vital Aire. S. Zhang and E. von Fintel report no disclosures relevant to the manuscript. T. Friede served in the past 3 years or serves currently as a consultant (including data monitoring committees and advisory boards) to Novartis, Biogen, Grünenthal, AstraZeneca, Bayer, Janssen, SGS, and Pharmalog. J. Lotz and J. Frahm report no disclosures relevant to the manuscript. J. Schmidt received honoraria, research grants, or reimbursements for travel from Bayer, Biogen, BioMarin, Biotest, CSL Behring, Grifols, Novartis, Ocatpharma, and Vital Aire. Go to Neurology.org for full disclosures.

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## REFERENCES

1. Carneiro D, das Graças Wanderley de Sales Coriolano M, Belo LR, de Marcos Rabelo AR, Asano AG, Lins OG. Quality of life related to swallowing in Parkinson's disease. *Dysphagia* 2014;29:578–582.
2. da Costa Franceschini A, Mourão L. Dysarthria and dysphagia in amyotrophic lateral sclerosis with spinal onset: a study of quality of life related to swallowing. *NeuroRehabilitation* 2015;36:127–134.
3. Logemann JA, Rademaker AW, Pauloski BR, Ohmae Y, Kahrilas PJ. Normal swallowing physiology as viewed by videofluoroscopy and videoendoscopy. *Folia Phoniatr Logop* 1998;50:311–319.
4. Langmore SE. Evaluation of oropharyngeal dysphagia: which diagnostic tool is superior? *Curr Opin Otolaryngol Head Neck Surg* 2003;11:485–489.
5. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. *Dysphagia* 1996;11:93–98.
6. Zhang S, Olthoff A, Frahm J. Real-time magnetic resonance imaging of normal swallowing. *J Magn Reson Imaging* 2012;35:1372–1379.
7. Olthoff A, Zhang S, Schweizer R, Frahm J. On the physiology of normal swallowing as revealed by magnetic resonance imaging in real time. *Gastroenterol Res Pract* 2014;2014:493174.
8. Cox FM, Verschuuren JJ, Verbist BM, Niks EH, Wintzen AR, Badrising UA. Detecting dysphagia in inclusion body myositis. *J Neurol* 2009;256:2009–2013.
9. Oh TH, Brumfield KA, Hoskin TL, et al. Dysphagia in inclusion body myositis: clinical features, management, and clinical outcome. *Am J Phys Med Rehabil* 2008;87:883–889.

10. Felice KJ, North WA. Inclusion body myositis in Connecticut: observations in 35 patients during an 8-year period. *Medicine* 2001;80:320–327.
11. Langdon PC, Mulcahy K, Shepherd KL, Low VH, Mastaglia FL. Pharyngeal dysphagia in inflammatory muscle diseases resulting from impaired suprahyoid musculature. *Dysphagia* 2012;27:408–417.
12. Rose M. 188th ENMC International Workshop: inclusion body myositis, 2–4 December 2011, Naarden, the Netherlands. *Neuromuscul Disord* 2013;23:1044–1055.
13. McHorney CA, Robbins J, Lomax K, et al. The SWAL-QOL and SWAL-CARE outcomes tool for oropharyngeal dysphagia in adults: III: documentation of reliability and validity. *Dysphagia* 2002;17:97–114.
14. Paris G, Martinaud O, Petit A, et al. Oropharyngeal dysphagia in amyotrophic lateral sclerosis alters quality of life. *J Oral Rehabil* 2013;40:199–204.
15. Leow LP, Huckabee ML, Anderson T, Beckert L. The impact of dysphagia on quality of life in ageing and Parkinson's disease as measured by the swallowing quality of life (SWAL-QOL) questionnaire. *Dysphagia* 2010;25:216–220.
16. Uecker M, Zhang S, Voit D, Karaus A, Merboldt KD, Frahm J. Real-time MRI at a resolution of 20 ms. *NMR Biomed* 2010;23:986–994.
17. Uecker M, Hohage T, Block KT, Frahm J. Image reconstruction by regularized nonlinear inversion: joint estimation of coil sensitivities and image content. *Magn Reson Med* 2008;60:674–682.
18. Zhang S, Block KT, Frahm J. Magnetic resonance imaging in real time: advances using radial FLASH. *J Magn Reson Imaging* 2010;31:101–109.
19. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.
20. Hayes AF, Krippendorff K. Answering the call for a standard reliability measure for coding data. *Commun Methods Meas* 2007;1:77–89.
21. Cassol K, Galli JF, Zamberlan NE, Dassi-Leite AP. Quality of life in swallowing in healthy elderly. *J Soc Bras Fonoaudiol* 2012;24:223–232.
22. Feinstein AR, Cicchetti DV. High agreement but low kappa: I: the problems of two paradoxes. *J Clin Epidemiol* 1990;43:543–549.
23. Pauloski BR, Logemann JA. Biomechanical analysis of the pharyngeal swallow in postsurgical patients with anterior tongue and floor of mouth resection and distal flap reconstruction. *J Speech Hear Res* 1995;38:110–123.
24. Sia I, Carvajal P, Carnaby-Mann GD, Crary MA. Measurement of hyoid and laryngeal displacement in video fluoroscopic swallowing studies: variability, reliability, and measurement error. *Dysphagia* 2012;27:192–197.
25. Inamoto Y, Fujii N, Saitoh E, et al. Evaluation of swallowing using 320-detector-row multislice CT: part II: kinematic analysis of laryngeal closure during normal swallowing. *Dysphagia* 2011;26:209–217.
26. Cox FM, Titulaer MJ, Sont JK, Wintzen AR, Verschuuren JJ, Badrising UA. A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities. *Brain* 2011;134:3167–3175.
27. Price MA, Barghout V, Benveniste O, et al. Mortality and causes of death in patients with sporadic inclusion body myositis: survey study based on the clinical experience of specialists in Australia, Europe and the USA. *J Neuromuscular Dis* 2016;3:67–75.
28. Baijens LWJ, Pilz W, Kremer B, Passos VL. Identifying patterns of FEES-derived swallowing trajectories using group-based trajectory model. *Dysphagia* 2015;30:529–539.
29. Murata KY, Kouda K, Tajima F, Kondo T. A dysphagia study in patients with sporadic inclusion body myositis (s-IBM). *Neurol Sci* 2012;33:765–770.
30. Miura Y, Nakagami G, Yabunaka K, et al. Method for detection of aspiration based on B-mode video ultrasonography. *Radiol Phys Technol* 2014;7:290–295.
31. Oh TH, Brumfield KA, Hoskin TL, Stolp KA, Murray JA, Bassford JR. Dysphagia in inflammatory myopathy: clinical characteristics, treatment strategies, and outcome in 62 patients. *Mayo Clin Proc* 2007;82:441–447.

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## Evaluation of dysphagia by novel real-time MRI

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## Supplementary Material:

### Table e-1: Overview of all data

Demographics, treatment, clinical and technical data of all patients. Clin.-pathol.: clinico-pathologically defined IBM; clinical: clinically defined IBM; prob.: probable IBM; Mup44: Autoantibody directed to cytosolic 5'-nucleotidase 1A (cN1A); MRC: Medical Research Council; IBM-FRS: IBM functional rating scale; sIFA: patient reported functional assessment for patients with IBM; SWAL-QoL: swallowing quality of life scale; RT-MRI: real-time magnetic resonance imaging; VF: videofluoroscopy; FEES: flexible endoscopic evaluation of swallowing; OTT: oral transit time; EOT: esophageal opening time; PTT: pharyngeal transit time; CP: cricopharyngeal propulsion; n.v.: no value (due to technical impairments, one VF and one FEES had to be excluded and laryngeal elevation could not be analyzed in one RT-MRI and CP could not be analyzed in two RT-MRI).

### Figure e-1: Correlation of functional IBM scale and MRC score with swallowing scale.

A statistically significant correlation was noted between the impairment of daily life activity per IBM-FRS and the muscle strength per clinical examination (MRC sum-score) (**A**) as well as between an impaired swallowing per swallowing quality of life scale (SWAL-QoL) and IBM-FRS (**B**). (normal values: IBM-FRS= 40, MRC= 140, SWAL-QoL= 100; sIFA= 0; degree of retention per RT-MRI/VF/FEES= 3; 0= most severe impairment in all scales except for the sIFA [max. severity= 110]).

### Figure e-2: Quantitative assessment of RT-MRI

**A)** Quantitative analysis of real-time MRI of swallowing in IBM patients shows a significantly prolonged oral transit time and esophageal opening time compared to healthy non-dysphagic controls (<sup>#</sup>reference values from<sup>6</sup>). The values for the pharyngeal transit time are borderline. Statistical analysis was performed by t-test as detailed in the Methods section. **B)** Significant correlation between the extent of the cricopharyngeal propulsion and the pharyngeal transit time. Exclusion of two data sets was required due to technical impairment of one VF and one FEES. OTT: oral transit time; PTT: pharyngeal transit time; EOT: esophageal opening time.

**Table e-1**

General parameters								Clinical data				Degree of retention per technical examinations (arbitrary score)			Additional information provided by RT-MRI				
#	Sex	Age	Years since onset	Mobility	Diagnostic Confidence	Mup44 (cN1A)	Treatment	MRC	IBM-FRS	SWAL-QoL	sIFA	RT-MRI	VF	FEES	OTT [ms, mean]	EOT [ms, mean]	PTT [ms, mean]	Laryngeal elevation [mm]	Extent of CP [mm]
1	m	74	10	Cane	clin.-pathol.	+	IVIG	111	28	77	26	2.5	2	1	371	247	618	27.6	8.2
2	f	71	8	Independent	clinical	+++	IVIG	131	27	59	67	2	1	n.v.	618	309	1567	40.7	8.6
3	f	79	10	Wheelchair	clin.-pathol.	+++	None	62	6	50	102	0	0.5	1.5	969	309	7174	33.1	9.0
4	m	83	12	Rollator	prob.	-	IVIG	95	11	29	74	2	2	0.5	247	371	1031	47.8	6.4
5	m	77	8	Independent	clin.-pathol.	-	None	137	36	99	29	3	2	3	275	371	673	46.9	2.3
6	m	63	6	Independent	prob.	-	Prednisone	124	30	96	47	2.5	2.5	2.5	371	302	728	25.8	4.5
7	f	75	8	Rollator, partly wheelchair	clinical	-	IVIG	99	13	93	91	3	2.5	2	268	289	515	21.4	3.0
8	m	78	16	Rollator, partly wheelchair	clinical	-	IVIG	95	13	59	84	1.5	0	3	440	344	1746	18.0	n.v.
9	f	77	14	Wheelchair, partly rollator	clinical	+++	IVIG	86	18	30	96	0	0	1	288	288	3876	19.3	0
10	m	70	12	Rollator, cane	clinical	-	IVIG	125	27	85	49	2	2.5	3	220	357	1058	33.8	6.4
11	m	72	5	Independent	prob.	+++	IVIG	136	31	86	43	2.5	n.v.	3	412	371	866	26.5	0
12	m	80	9	Rollator, partly wheelchair	clin.-pathol.	+	IVIG	112	23	69	83	1	0.5	1	354	247	2639	33.4	9.0
13	m	65	9	Independent	clin.-pathol.	-	IVIG	121	18	52	91	2	2.5	0.5	329	274	1030	25.1	0
14	f	73	6	Rollator	clin.-pathol.	+	IVIG	132	29	85	47	1	2	1	412	268	721	23.5	3.6
15	m	72	5	Independent	clin.-pathol.	-	IVIG	131	24	46	77	1	0.5	1	268	227	722	37.2	n.v.
16	f	85	12	Wheelchair	clinical	-	IVIG	101	21	56	93	1	1	2	894	474	2453	25.8	10.5
17	m	59	19	Independent	prob.	-	None	80	16	55	90	2	1	0	384	247	1264	23.1	5.2
18	f	67	6	Independent	prob.	++	IVIG	120	35	87	11	2	1.5	0.5	467	412	1278	29.4	5.6
19	f	71	12	Independent	clin.-pathol.	-	IVIG, Azathioprine	114	30	50	60	3	2	1	302	391	824	26.9	3.7
20	m	65	4	Cane	clin.-pathol.	+++	IVIG	115	27	93	61	2	1.5	1	329	371	797	44.3	6.5

Figure e-1

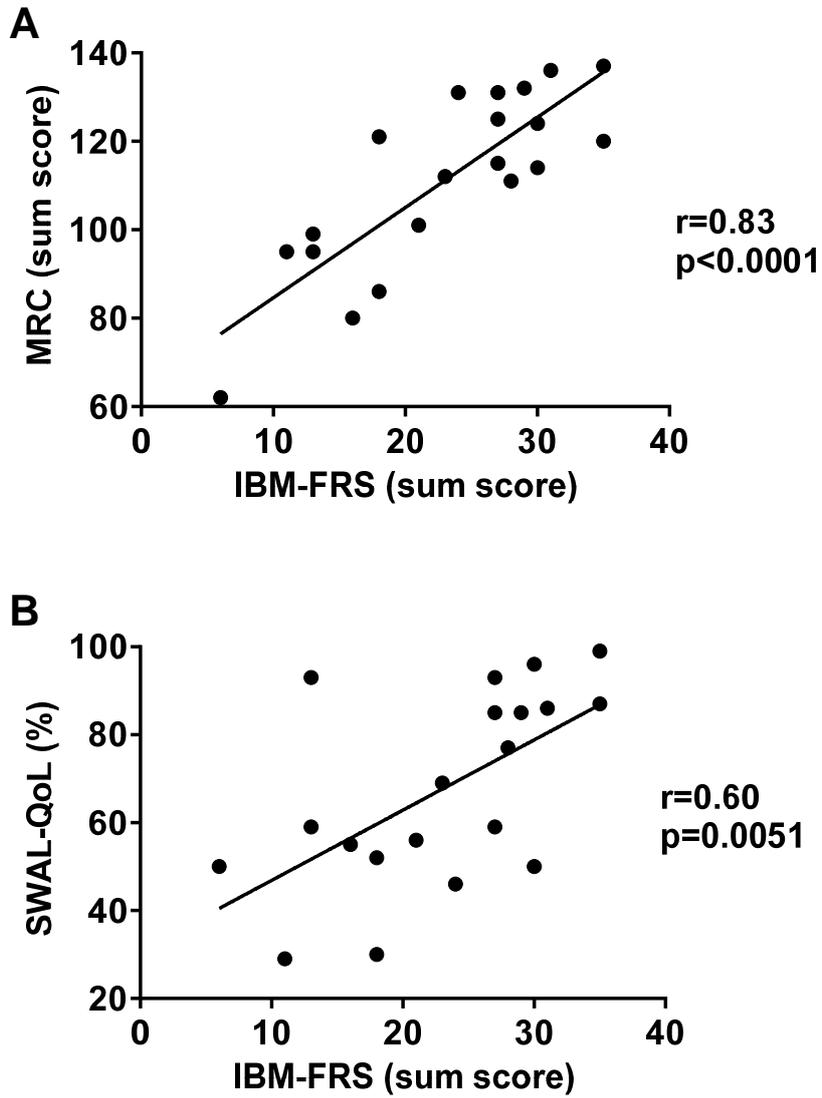
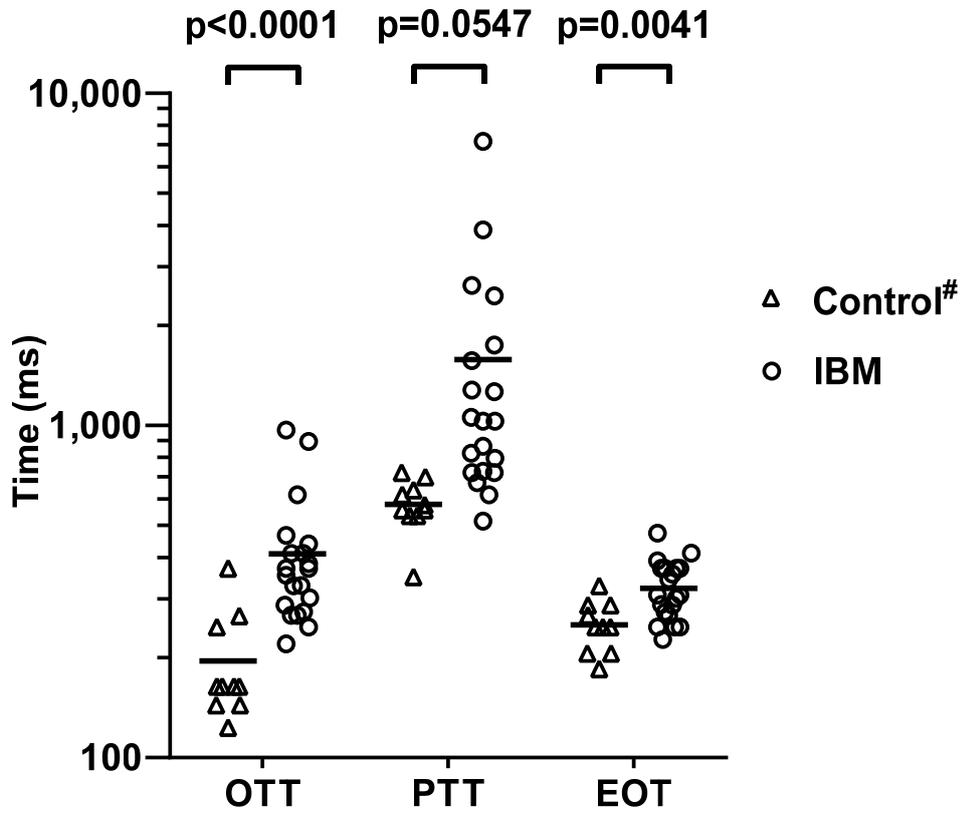
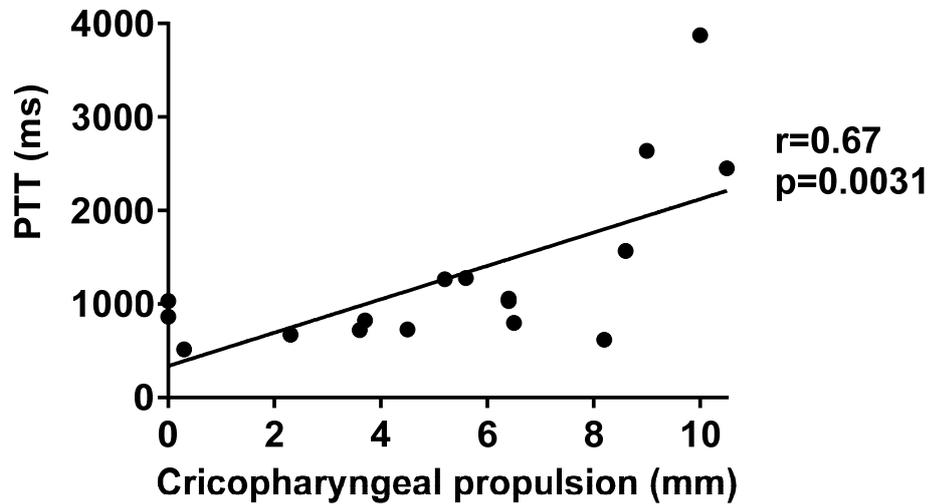


Figure e-2

A



B



**Videos 1 to 6:**

The movies show exemplary findings of swallowing in patients with IBM: Normal swallowing (Video 1) and dysphagia (Video 2) in RT-MRI; Normal swallowing (Video 3) and dysphagia (Video 4) in VF; Normal swallowing (Video 5) and dysphagia (Video 6) in FEES.

**Video 1:** Normal swallowing – RT-MRI

**Video 2:** Relevant dysphagia – RT-MRI

**Video 3:** Normal swallowing – VF

**Video 4:** Relevant dysphagia – VF

**Video 5:** Normal swallowing – FEES

**Video 6:** Relevant dysphagia – FEES