NEUROLOGIE und MS

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MS-MRT-Kriterien: Hintergrund

- MRT: wichtigster "paraklinischer" Diagnoseparameter für Multiple Sklerose (MS)
- Konzept von Dissemination im Raum (DIS) und in der Zeit (DIT)
- Ein klinisches Ereignis und positives MRT:
  - Diagnosestellung der MS
  - Frühzeitige Behandlung
  - Sensitivität der MRT hat Einfluß auf die Therapie

MR-Kriterien für MS

- Anzahl der Entmarkungsherde *(Läsionen)*
- Lokalisation der Entmarkungsherde
  (periventrikulär, subkortikal = kortikomedullär / kortikal, infratentoriell, Optikus)
- Kontrastmittelaufnahme
- Örtliche *(= räumliche)* und zeitliche Dissemination

DIS:

Dissemination In Space

MAGNIMS 2016 vs. McDonald 2017: ≥ 2 von 5/4 DIS-Kriterien

1. ≥3 periventrikuläre Läsionen:
   bei McDonald 2017 nur ≥ 1
   "unless the patient is over the age of 50 in which case it is advised to seek a higher number of lesions"
2. ≥1 kortikale / subkortikale (= kortikomedulläre) Läsion
3. ≥1 infratentorielle Läsion
4. ≥1 spinale Läsion
5. ≥1 Optikusentmarkung:
   nicht Teil der 2017 rev. McDonald-Kriterien

MAGNIMS - **MAGN**etic Resonance **I**maging in **M**ultiple **S**clerosis, *European Collaborative Research Network*

Ian McDonald (1933-2006) – *neuseeländischer Neurologe, der die Kriterien federführend 2001 einführte*

DIT:

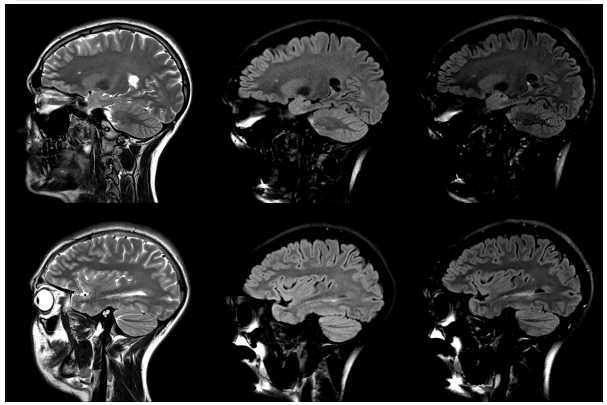
Dissemination In Time

u.a. zur Abgrenzung von monophasischen entzündlichen ZNS-Erkrankungen wie ADEM

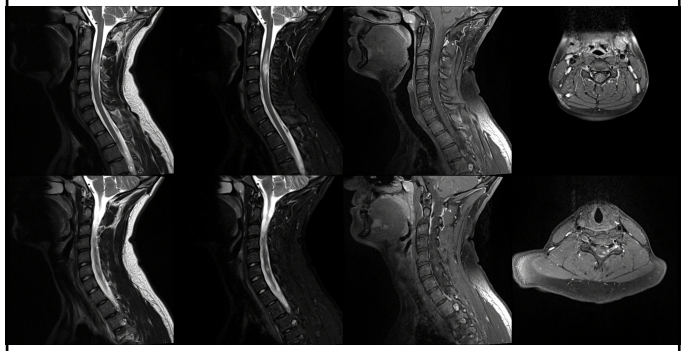
DIT: MAGNIMS 2016 = McDonald 2017

1. ≥ 1 zu vorherigem MRT neue Entmarkung (T2 ± KM-Anreicherung; egal wann)
2. gleichzeitige Detektion einer nicht anreichernden und einer KM aufnehmenden Entmarkung

Fall 1, ♂, jetzt 19 a
cMRTs 04/2018, 06/2020 u. 02/2021

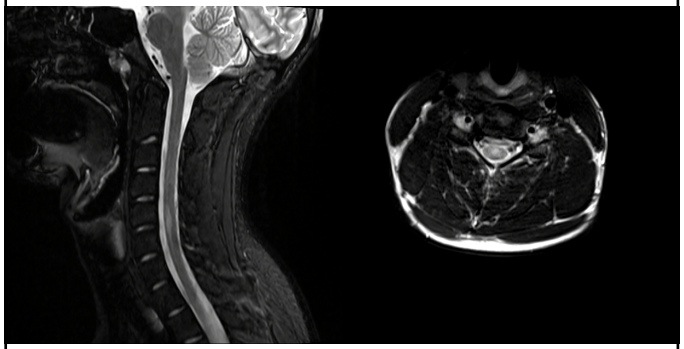


Fall 1, ♂, mit 16 a, MS oder NMO-SD ?
sMRT 04/2018: DIS McDonald +?/MAGNIMS -



- Klinisch: Hemiparese rechts, Sensibilitätsausfälle rechter Arm

Fall 1, ♂, mit 18 a
sMRT 12/2019: DIT + / +



Fall 1, ♂, 19 a
Klinisch und Therapie

Diagnosen: **schubförmige Multiple Sklerose + ADHS**

- **zervikale Myelitis 4/2018**
  - Sensibilitätsstörung und Kraftminderung im rechten Arm, im Verlauf auch im rechten Bein + entzündliches Liquorsyndrom
  - Keine RBN
- unter Copaxone 5/2018 bis 9/2019
- Umstellung wg Spritzenphobie auf Aubagio von 9/2019 bis 2/2020
- Zervikal neuer Herd 12/2019 und Schwäche im rechten Arm – im Verlauf Zunahme der Paresen und starke Spastik
- Tysabri seit 5.3.2020, heute 13. Infusion – klinisch und MR-tomografisch stabil

MS-Diagnose – Wann?

Diagnose und Therapie der Multiplen Sklerose, Neuromyelitis-optica-Spektrum-Erkrankungen und MOG-IgG-assoziierten Erkrankungen

DGN Deutsche Gesellschaft für Neurologie

Schubförmige MS

Zahl der Schübe	objektive Läsionen	zusätzlich erforderliche Kriterien
2 oder mehr	2 oder mehr	keine
2 oder mehr	1	DIS: weiterer Schub mit objektiver Läsion *oder* DIS-MRT*
1	2 oder mehr	DIT: weiterer Schub oder DIT-MRT** *oder* OKB
1	1	DIS *und* DIT

Thompson et al., 2018

Primär progrediente MS (PPMS)

Klinische Progression über *mindestens 1 Jahr* (prospektiv oder retrospektiv)
und zwei der folgenden Kriterien:

- mind. eine T2-hyperintense Läsion# in mindestens einem der Areale *periventrikulär, kortikal/juxtakortikal* oder *infratentoriell*
- mind. zwei T2-hyperintense Läsionen# *spinal*
- Nachweis liquorspezifischer oligoklonaler Banden

#symptomatische und asymptomatische Läsionen zählen gleichermaßen

Thompson et al., 2018

MAGNIMS 2016 vs. McDonald 2017 und Neuerungen:

- **RBN als eigenständiges MRT-Kriterium**
  (ca. 25% mit CIS kommen mit RBN)
- **≥ 3 vs. 1 periventrikuläre Entmarkungsherde**
  (Sensitivität vs. Spezifität, pV+)
- **auch kortikale statt nur juxtakortikale Lokalisation**
- **sowohl symptomatische als auch „stille“ Läsionen werden für DIS & DIT berücksichtigt**

MRT-Stellenwert für MS-Diagnostik

- Sensitivität für Entwicklung MS nach 1 Jahr
  - 74-83%
- Spezifität für Entwicklung MS nach 1 Jahr
  - 83-86%

(prä-MAGNIMS: Dalton et al., 2002, Tintore et al., 2003)

MRT liefert einen wichtigen Beitrag zur Frühdiagnose der Multiplen Sklerose

ABER:

- **Keine echte „differentia specifica“**

Neurology 87:1393-1399, 2016

The contemporary spectrum of multiple sclerosis misdiagnosis

A multicenter study

18

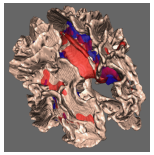
Stellenwert des MRT im MS-Verlauf- und -Therapiemonitoring

- DMT-Therapieziel: „no evidence of disease activity“ = klinische Stabilität, keine neuen Herde, keine inadäquat akzellerierte Atrophie (NEDA-IV)
- Erkennen von Komplikationen (PML, IRIS etc.)

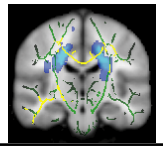
MRT liefert wichtigen Beitrag zur Verlaufsbeurteilung der MS, beim Therapiemonitoring und in der Pharmakovigilanz

Was wird *(noch)* nicht *(adäquat)* berücksichtigt?

- **Volumen der Entmarkungen**
- **Zerebrale und spinale Atrophie (neurodegenerative Komponente)**



- **Läsionsmikrostruktur (Myelin!), quantitative Relaxometrie / Diffusion** (z.B. TBSS) **/ Spektroskopie**



Wie soll MS-MRT erfolgen ?

- **Bindende KV-Vorgaben**
- **2021 MAGNIMS-CMSC-NAIMS Empfehlungen**

(Lancet Neurol https://doi.org/10.1016/S1474-4422(21)00095-8)

CMSC – Consortium of Multiple Sclerosis Centres

NAIMS – North American Imaging in Multiple Sclerosis Cooperative

KV-Vorgaben 2020

Richtlinie

Gemeinsamer Bundesausschuss

des Gemeinsamen Bundesausschusses über Kriterien zur Qualitätsbeurteilung in der Kernspintomographie nach § 135b Absatz 2 SGB V

(Qualitätsbeurteilungs-Richtlinie Kernspintomographie/QBK-RL)

in der Fassung vom 17. Oktober 2019
veröffentlicht im Bundesanzeiger (BAnz AT 30.01.2020 B3)
in Kraft getreten am 1. Januar 2020

MS-MRT nach QBK-RL 2020

- nur Neurokranium geregelt, *nicht Myelon oder Optikus*
- keine Empfehlung zur *Feldstärke*
- i.v. KM: *obligat* zur *Diagnosestellung* bei Erstmanifestation; *fakultativ* zur *Verlaufskontrolle* (mindestens 5 Minuten vor T1 Gd), *Darstellung in zwei Ebenen*
- 2D: 1x1x*5mm*, 3D: *1.5mm* isotrop, *FoV 250mm*
- axial T2-FLAIR und T1 und *sagittal T2 oder* axial T2.PD und T1 und *sagittal T2*
- Referenzstrukturen: GM/WM, *fokale Läsionen >3mm, T1-hypointense Läsionen („black holes"), KM-anreichernde bzw. neue Läsionen im Verlauf, DIS / DIT*

MS-MRT nach MAGNIMS(-CMSC-NAIMS) 2021

Position Paper

2021 MAGNIMS–CMSC–NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

*Mike P Wattjes, Olga Ciccarelli, Daniel S Reich, Brenda Banwell, Nicola de Stefano, Christian Enzinger, Franz Fazekas, Massimo Filippi, Jette Frederiksen, Claudia Gasperini, Yael Hacohen, Ludwig Kappos, David K B Li, Kshitij Mankad, Xavier Montalban, Scott D Newsome, Jiwon Oh, Jacqueline Palace, Maria A Rocca, Jaume Sastre-Garriga, Mar Tintoré, Anthony Traboulsee, Hugo Vrenken, Tarek Yousry, Frederik Barkhof, Àlex Rovira on behalf of the Magnetic Resonance Imaging in Multiple Sclerosis study group, the Consortium of Multiple Sclerosis Centres, and North American Imaging in Multiple Sclerosis Cooperative MRI guidelines working group**

The 2015 Magnetic Resonance Imaging in Multiple Sclerosis and 2016 Consortium of Multiple Sclerosis Centres guidelines on the use of MRI in diagnosis and monitoring of multiple sclerosis made an important step towards appropriate use of MRI in routine clinical practice. Since their promulgation, there have been substantial relevant advances in knowledge, including the 2017 revisions of the McDonald diagnostic criteria, renewed safety concerns regarding intravenous gadolinium-based contrast agents, and the value of spinal cord MRI for diagnostic, prognostic, and monitoring purposes. These developments suggest a changing role of MRI for the management of patients with multiple sclerosis. This 2021 revision of the previous guidelines on MRI use for patients with multiple sclerosis merges recommendations from the Magnetic Resonance Imaging in Multiple Sclerosis study group, Consortium of Multiple Sclerosis Centres, and North American Imaging in Multiple Sclerosis Cooperative, and translates research findings into clinical practice to improve the use of MRI for diagnosis, prognosis, and monitoring of individuals with multiple sclerosis. We recommend changes in MRI acquisition protocols, such as emphasising the value of three dimensional fluid-attenuated inversion recovery as the core brain pulse sequence to improve diagnostic accuracy and ability to identify new lesions to monitor treatment effectiveness, and we provide recommendations for the judicious use of gadolinium-based contrast agents for specific clinical purposes. Additionally, we extend the recommendations to the use of MRI in patients with multiple sclerosis in childhood, during pregnancy, and in the post-partum period. Finally, we discuss promising MRI approaches that might deserve introduction into clinical practice in the near future.

Lancet Neurol 2021
Published Online June 14, 2021
https://doi.org/10.1016/S1474-4422(21)00095-8

*Members are listed in the appendix
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MS-MRT nach MAGNIMS(-CMSC-NAIMS) 2021

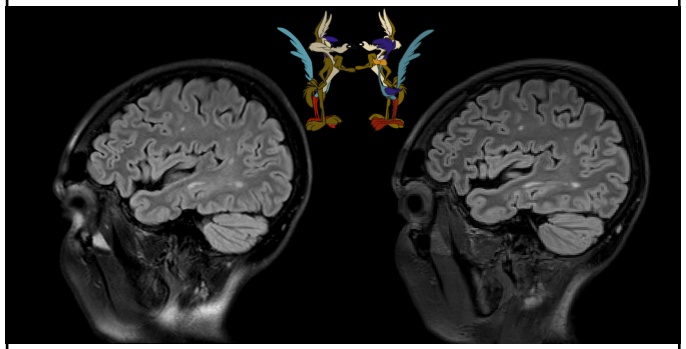
	Brain	Spinal cord	Optic nerve
Field strength	≥1·5 T (preferably 3 T)	≥1·5 T (3 T has no added value compared with 1·5 T)	≥1·5 T
Slice thickness	For 3D imaging, 1 mm isotropic is preferred but, if over contiguous (through plane and in plane), not >1·5 mm, with 0·75 mm overlap; for 2D imaging, ≤3 mm with no gap (except for diffusion-weighted imaging, for which the slice thickness should be ≤5 mm with a 10–30% gap)	Sagittal slices should be ≤3 mm with no gap; axial slices should be ≤5 mm with no gap	≤2–3 mm with no gap
In-plane resolution	≤1 mm × 1 mm	≤1 mm × 1 mm	≤1 mm × 1 mm
Coverage	Whole brain (include as much of cervical cord as possible)	Cervical and thoracolumbar spinal cord, to include conus	Optic nerve and optic chiasm
Axial scan orientation	Subcallosal plane to prescribe (ie, for 2D imaging) or reformat (ie, for 3D imaging) axial oblique slices	Perpendicular to the sagittal axis of the spinal cord	Aligned to the orientation of the optic nerve and optic chiasm

3D=three dimensional. 2D=two dimensional.

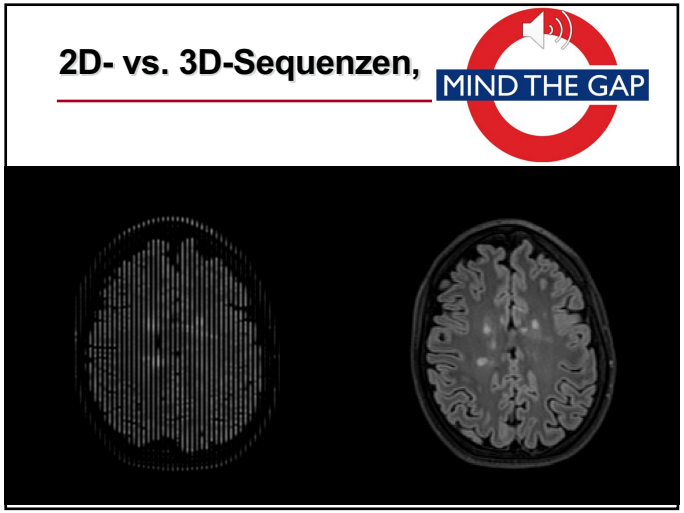
Table 1: Basic MRI parameters

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

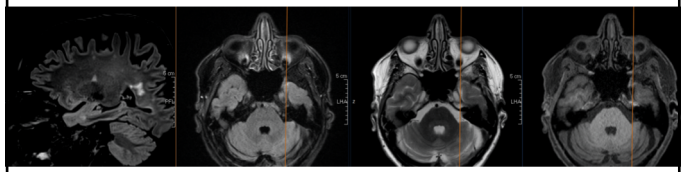
2D- vs. 3D-Sequenzen: Vor- und Nachteile



2D- vs. 3D-Sequenzen,



3D-Sequenzen: Immer besser?



	Multiple sclerosis diagnosis	Assessment of disease activity and monitoring effectiveness of the disease-modifying treatment*	Safety monitoring for disease-modifying treatment (eg, progressive multifocal leukoencephalopathy screening)
Brain MRI protocol			
Axial T2-weighted (TSE or FSE) sequences†	Recommended	Recommended (optional if high-quality sagittal 3D T2-weighted FLAIR and multiplanar reconstruction in axial and sagittal planes are available)	Recommended (optional if high-quality sagittal 3D T2-weighted FLAIR and multiplanar reconstruction in axial and sagittal planes are available)
Sagittal T2-weighted FLAIR (preferably 3D; fat suppression is optional)	Recommended	Recommended	Recommended
Axial T2-weighted FLAIR (unnecessary if a sagittal 3D FLAIR with multiplanar reconstruction is obtained; fat suppression is optional)	Recommended	Recommended	Recommended
Axial (or 3D sagittal) T1-weighted sequences after contrast‡	Recommended	Optional	Optional
Diffusion-weighted imaging	Optional	Optional (should be considered for differential diagnosis)	Recommended
Double inversion recovery or PSIR for detecting cortical or juxtacortical lesions	Optional	Optional	Optional
High-resolution T1-weighted sequences (isotropic 3D acquisition; for quantitative assessment of brain volume)	Optional	Optional	Not required
Susceptibility-weighted imaging	Optional for assessing the central vein sign	Not required	Not required
Optic nerve MRI protocol			
Axial and coronal fat-suppressed T2-weighted sequences or STIR of optic nerve	Optional (can be considered in some clinical situations; 2D or 3D acquisition)	Not required	Not required
Axial and coronal fat-suppressed T1-weighted sequences post contrast of optic nerve	Optional (can be considered in some clinical situations; 2D or 3D acquisition)	Not required	Not required
Spinal cord MRI protocol			
At least two of: sagittal T2-weighted sequences (TSE or FSE), proton density-weighted sequences (TSE or FSE), or STIR	Recommended	Optional	Not required
Sagittal 3D heavily T1-weighted sequences (PSIR or magnetisation-prepared rapid acquisition of gradient echoes§) only for the cervical segment	Optional	Optional	Not required
Axial T2-weighted (TSE or FSE) or gradient-recalled echo to corroborate, characterise, and confirm lesions detected on sagittal images or to detect lesions in spinal cord segments with high clinical suspicions of involvement	Optional	Optional	Not required
Sagittal T1-weighted sequences (TSE or FSE) before contrast	Optional	Optional	Not required
Sagittal T1-weighted sequences (TSE or FSE) after contrast‡	Recommended	Optional	Not required
Axial T1-weighted sequences (TSE or FSE) after contrast‡	Optional	Optional	Not required

TSE=turbo spin echo. FSE=fast spin echo. FLAIR=fluid attenuated inversion recovery. PSIR=phase sensitive inversion recovery. STIR=short tau inversion recovery. *Spinal cord MRI for assessing treatment efficacy and monitoring disease activity is not recommended on a regular basis but is advised for special clinical conditions only. †A dual-echo (proton density-weighted and T2-weighted) sequence can be considered as an alternative to a single echo T2-weighted sequence. ‡Standard doses of 0·1 mmol/kg bodyweight, macrocyclic gadolinium chelates only, with a minimum delay of 5–10 min. §One of these sequences could replace T2-weighted sequences, proton density-weighted sequences, or short tau inversion recovery.

Table 2: **Standardised brain, optic nerve, and spinal MRI protocols**

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

Panel 1: Magnetic Resonance Imaging in Multiple Sclerosis-Consortium of Multiple Sclerosis Centres-North American Imaging in Multiple Sclerosis Cooperative recommendations for the use of MRI for establishing multiple sclerosis diagnosis

Standardised initial brain protocol:
- At least 1·5 T; 3 T if available
- Acquisition and interpretation of 7 T images for clinical routine purposes require dedicated expertise
- Core sequences are: T2-weighted 3D-fluid-attenuated inversion recovery, axial T2-weighted, and T1-weighted with gadolinium (table 2)
- Precontrast T1-weighted sequences are not required

Standardised initial spinal cord protocol:
- 1·5 T or 3 T
- Details on pulse sequences can be found in table 2

Additional or advanced MRI:
- Diffusion-weighted imaging cannot replace gadolinium as a marker for active inflammation
- Dedicated optic nerve MRI is not recommended except for differential diagnosis with neuromyelitis optica spectrum disorders and in patients with atypical clinical features
- There is insufficient current evidence or widespread technology availability to recommend routine use of quantitative MRI techniques and brain volumetric measurements, double inversion recovery or phase-sensitive inversion recovery for cortical lesions, and central vein sign and paramagnetic rims as diagnostic markers

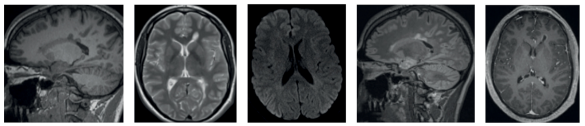
Follow up imaging to establish multiple sclerosis diagnosis when the first MRI does not fulfill the criteria:
- Brain MRI is recommended every 6–12 months in clinically isolated syndrome and subclinical multiple sclerosis radiologically isolated syndrome with risk factors for conversion to multiple sclerosis and paraclinical features of multiple sclerosis
- Spinal cord MRI is not routinely recommended
- Use of gadolinium is not recommended
- Identical image acquisition (ie, standardised repositioning, field strength, pulse sequences, spatial resolution) is strongly recommended

Image interpretation:
- Standardised image interpretation and reporting is recommended
- Knowledge about definition of lesion types is crucial and warning signs against a diagnosis of multiple sclerosis should be recognised
- Standard measures, such as T2 lesion count (ie, if less than 20 T2 lesions in the brain, then provide the exact number, and otherwise report an estimate of between 20 and 50 lesions, between 50 and 100 lesions, more than 100 lesions, or uncountable [ie, confluent] lesions; if <10 lesions in the spinal cord, then provide the exact number, otherwise report more than 10 lesions or diffuse pattern) and gadolinium-enhancing lesion count if gadolinium was administered, are recommended
- Separate identification of cortical lesions (together with juxtacortical lesions) based on standard images (eg, fluid-attenuated inversion recovery; double inversion recovery or phase-sensitive inversion recovery sequences are optional) is recommended

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MS-MRT nach MAGNIMS(-CMSC-NAIMS) 2021

3D T1-weighted (optional)	2D turbo spin echo T2-weighted*	Diffusion-weighted imaging (optional)†	3D T2-weighted FLAIR‡	2D or 3D contrast-enhanced T1-weighted (optional)



Contrast injection in selected cases§

Minimum delay 5–10 min

Figure 1: **Recommended brain MRI protocol**
In selected cases, contrast agent can be injected just before the 3D T2-weighted FLAIR; the delay to the start of the 2D or 3D contrast-enhanced T1-weighted imaging should be a minimum of 5–10 min. Spatial resolution parameters for 3D sequences are ≤1 mm × 1 mm × 1 mm (ie, multiplanar reconstruction 3 mm). Spatial resolution parameters for 2D sequences are ≤1 mm × 1 mm × ≤3 mm (table 1). 3D=three dimensional. 2D=two dimensional. FLAIR=fluid-attenuated inversion recovery. *Either single or dual echo. Can be skipped if there is good quality 3D FLAIR in the monitoring protocol. †For differential diagnosis. ‡Transverse 2D FLAIR could be considered as an alternative, if 3D-FLAIR not available or not of good quality. §0·1 mmol/kg bodyweight of macrocyclic agents.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MAGNIMS(-CMSC-NAIMS) 2021: Wann KM?

Panel 2: Recommendations on the use of gadolinium-based contrast agents in the diagnosis and monitoring of multiple sclerosis

Diagnosis

The use of gadolinium-based contrast agents is recommended:
- To show dissemination in time on the baseline MRI scan.
- To contribute to differential diagnosis (ie, on the basis of the pattern of enhancement).
- To predict future disease activity and to some extent disease progression.
- For phenotyping patients with progressive disease (ie, active or inactive), if a recent (ie, within 1 year) MRI is not available, and if this information affects treatment decisions.

No double/triple dose!

Monitoring

The use of gadolinium-based contrast agents is recommended:
- In the first year of follow-up (ie, after treatment initiation) if a new baseline MRI scan (ie, usually 3–6 months after treatment initiation) was not obtained, particularly in patients on interferon beta or glatiramer acetate (which are less effective in reducing MRI activity than are other therapies).
- If detection or confirmation of clinical disease activity is required in patients without a recent reference brain MRI scan (done ≤3–6 months ago). MRI should be ideally done as soon as possible and before steroid treatment.
- If showing disease activity with presence of gadolinium-enhancing lesions is required to initiate or change a specific disease-modifying treatment.
- In patients with diffuse and confluent chronic multiple sclerosis lesions (ie, large lesion burden), in which detection of disease activity is required but difficult to show on the basis of new or enlarged T2 lesions.
- For progressive multifocal leukoencephalopathy screening, if there has been a suspicious lesion detected on the standard monitoring or screening brain MRI scan.
- In monitoring of progressive multifocal leukoencephalopathy and detection and monitoring of progressive multifocal leukoencephalopathy-immune reconstitution inflammatory syndrome.

The use of gadolinium-based contrast agents is not recommended:
- To show dissemination in time on serial MRI scans. In case of standard monitoring for subclinical disease activity, if a previous and recent (ie, within approximately 1 year) MRI scan is available that was done with similar technical parameters.
- In new baseline (ie, usually 3–6 months after treatment initiation) MRI scan.
- In short follow-up MRI (ie, within 6 months) done to confirm disease activity in patients with isolated MRI activity on the previous MRI scan.
- For progressive multifocal leukoencephalopathy screening.
- During pregnancy (strictly contraindicated) and lactation (ie, indicated only if essential for patient management).

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

Fall 2, ♀, 38 a

Diagnosen:
Hochaktive Verlaufsform einer schubförmigen MS (EM 2/2007, aktuelle EDSS 2.0)

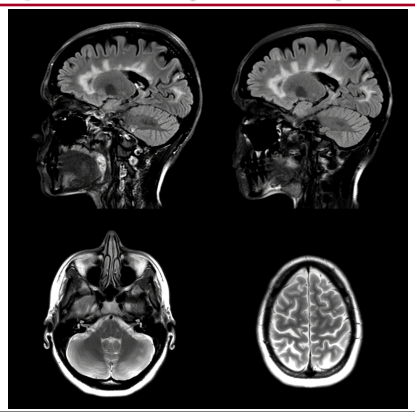
- Therapieversagen von Betaferon und Copaxone

- Tysabri Beginn 6/2014, Zustand nach 26 Infusionen
- Serokonversion mit Nachweis von JCV-AK 1/2016

- erster Lemtrada-Zyklus vom 14. bis 18.11.2016
- zweiter Lemtrada-Zyklus vom 21. bis 23.11.2017
- 3. Lemtrada-Zyklus vom 24. bis zum 26.3.2020

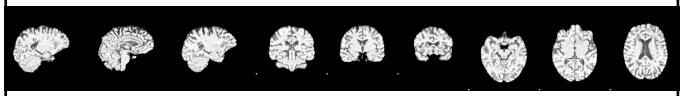
- **Erneut Schub und Nachweis von Entzündungsaktivität im cranialen und thorakalen MRT**
- **geplante Neueinstellung auf Ocrevus**

Fall 2, ♀, 38 a
02 vs. 04/21: Schub, Kortison, neuer Herd

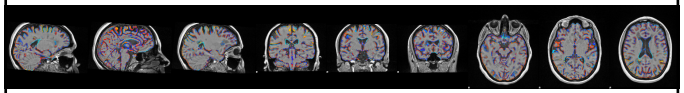


Fall 2, ♀, 38 a
2015-21: Atrophie? Schätzen Sie!

Hirn: PBVC = -0.90 %



Ventrikel: PVVC = +19.70 %



SIENA/VIENA, Teil von FSL; NeuroImage, 17(1):479-489, 2002

MAGNIMS(-CMSC-NAIMS) 2021: Spinal

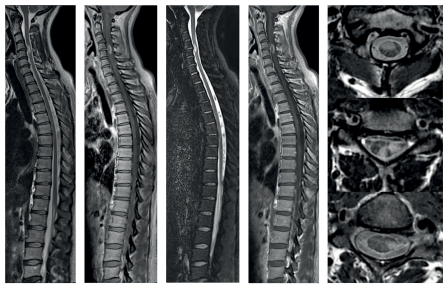


Figure 2: Recommended spinal cord MRI protocol
In selected cases, contrast agent can be injected just before the 2D T2-weighted sequence; the time to the end of the 2D contrast-enhanced T1-weighted imaging should be a minimum of 5–10 min. 2D=two dimensional. TSE=turbo spin echo. *Select proton density-weighted sequences or short tau inversion recovery. †Only in selected cases and, if possible, after acquisition of the contrast-enhanced brain MRI (ie, if contrast-enhanced MRI is to be used for both brain and spinal cord, the spinal cord contrast-enhanced T1-weighted sequence should come immediately after the brain contrast-enhanced T1-weighted sequence; minimum delay 5–10 min). ‡Only in selected cases. §0·1 mmol/kg bodyweight of macrocyclic agents.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MAGNIMS 2021: Spinal + Optikus

Panel 3: **Indications and objectives for use of spinal cord and optic nerve imaging for diagnosis, prognosis, and monitoring**

Spinal cord

Diagnosis

Clinically isolated syndrome establishing the diagnosis according to 2017 McDonald criteria[4]
- Detection of symptomatic or asymptomatic spinal cord lesions to show dissemination in space and time

Clinically isolated syndrome: differential diagnosis in case of inconclusive brain MRI findings
- Presence of typical demyelinating spinal cord lesions
- Exclusion of alternative diagnosis (eg, neuromyelitis optica spectrum disorders and MOG-antibody-associated disease)

Primary progressive multiple sclerosis establishing the diagnosis
- Detection of typical demyelinating spinal cord lesions to show dissemination in space
- Detection of diffuse lesions (ie, diffuse abnormal areas of intermediate signal intensity on proton density-weighted or short tau inversion recovery sequences without a well demarcated border)
- Exclusion of alternative diagnosis (eg, compressive myelopathy)

Prognosis

Radiologically isolated syndrome: prediction of clinically isolated syndrome or multiple sclerosis development
- Detection of asymptomatic spinal cord lesions

Clinically isolated syndrome or early multiple sclerosis: prediction of disability, disability progression, and development of secondary progressive multiple sclerosis
- Detection of spinal cord lesions (ie, active lesions on follow-up MRI scans)

Monitoring

Patients with multiple sclerosis and spinal cord phenotype (ie, no or few brain lesions)
- Detection of active spinal cord lesions

Patients with multiple sclerosis and disability worsening that cannot be explained by brain MRI
- Detection of active spinal cord lesions
- Exclusion of possible comorbidity involving the spine or spinal cord

Patients with multiple sclerosis and repeated spinal cord relapse
- Detection of active spinal cord lesions
- Exclusion of alternative diagnosis or possible comorbidity involving the spinal cord

Treatment switch decision making: inconclusive clinical presentation or brain MRI findings
- Detection of active spinal cord lesions
- Exclusion of possible comorbidity involving the spinal cord

Atypical spinal cord relapse or atypical spinal cord symptoms or signs suggestive of comorbidity
- Detection of active spinal cord lesions
- Exclusion of alternative diagnosis or possible comorbidity involving the spinal cord

Optic nerve

Diagnosis

Clinically isolated syndrome: differential diagnosis
- Atypical isolated optic neuritis; relapsing isolated optic neuritis; chronic relapsing inflammatory optic neuropathy
- Other diseases or factors affecting the optic nerve (eg, neuromyelitis optica spectrum disorders, infectious diseases, vaccination, sarcoidosis, tumours, etc)

Optic neuritis in paediatric patients
- Exclusion of alternative diagnosis (eg, neuromyelitis optica spectrum disorders and MOG-antibody-associated demyelination)

Monitoring
- Patients with multiple sclerosis and new visual symptoms that are suggestive of comorbidity affecting the optic nerve
- Patients with multiple sclerosis and chronic progressive optic nerve symptoms
- Patients with multiple sclerosis and repeated isolated optic nerve relapses

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MAGNIMS 2021: Spinal + Optikus

Panel 4: **Magnetic Resonance Imaging in Multiple Sclerosis–Consortium of Multiple Sclerosis Centres–North American Imaging in Multiple Sclerosis Cooperative recommendations for the use of MRI for monitoring treatment effectiveness and assessment of disease activity**

MRI timing

Obtain a baseline brain MRI (with gadolinium if required by drug label) before starting or switching disease-modifying treatment.

Obtain a new baseline brain MRI usually at 3–6 months after treatment onset to avoid misinterpretation of lesions that developed before therapeutic onset. Longer intervals are to be considered in patients who are treated with disease-modifying therapies that are slow acting.

Obtain a new baseline MRI usually at 3–6 months after treatment initiation without gadolinium unless highly active disease at baseline or unexpected clinical activity.

Consider gadolinium-enhanced MRI on first follow-up scan after treatment initiation in the absence of a new baseline scan.

Obtain yearly brain MRI while the patient is on the disease-modifying treatment; consider longer intervals in clinically stable patients after the first few years of treatment, particularly if safety monitoring is not required.

In patients who show MRI disease activity that is not associated with clinical activity on a follow-up scan, consider a new MRI scan without gadolinium 6 months later.

MRI acquisition

Identical slice positioning, pulse sequences, magnetic field strengths, and spatial resolution are highly recommended. Brain MRI should be done according to the standardised acquisition protocol (tables 1, 2).

- Abbreviated MRI protocol (ie, 3D T2-weighted fluid-attenuated inversion recovery; optional gadolinium-enhanced T1-weighted sequences) can be sufficient.
- Use of gadolinium-based contrast agents is optional and not recommended for all clinical situations (ie, consider new or enlarging T2 lesions as the only measure when a recent [ie, ≤1 year] reference scan is available); use gadolinium judiciously; minimise repeated gadolinium imaging when possible and use a single dose (table 2, panel 2).

Spinal cord MRI is not routinely recommended to detect subclinical activity; in clinical situations requiring spinal cord MRI (panel 3), images should be acquired according to a high-quality standardised protocol (tables 1, 2).

Optic nerve MRI is not routinely recommended to detect subclinical activity. In clinical situations requiring optic nerve MRI (panel 3), images should be acquired according to a high-quality standardised protocol (tables 1, 2).

MRI reporting in the clinical setting

Report active (new or enlarging) T2 lesions.

Co-registration, fusion, and subtraction techniques are helpful, especially if T2 lesion load is high.

Recognise poor sensitivity of routine MRI for cortical grey matter lesions.

Focal leptomeningeal gadolinium-enhancement cannot yet be considered a reliable marker for active inflammatory disease activity.

Volumetric and quantitative MRI measures, including commercially approved automated segmentation techniques, are not routinely recommended.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

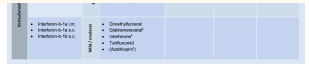
Neue Leitlinien zur Behandlung der Multiplen Sklerose

1. DGN S2k Leitlinie: „Eskalationsprinzip“

2. Multiple Sklerose Therapie Konsensus Gruppe „Frühe Therapie mit aktiv wirksamen Medikament“

Therapieempfehlung

1. Früh im Krankheitsverlauf
2. Auf den Patienten und den Krankheitsverlauf optimal wirksame Therapie



Der Nervenarzt
Konsensusgruppe

White Paper - Empfehlungen

1. Welchen Nutzen hat eine DMT bei Patienten mit KIS, unabhängig davon, ob sie die Kriterien einer definitiven MS erfüllen, im Vergleich zu keiner Behandlung?

Empfehlung 1:

Die Auswahl der Immuntherapie sollte sich an den prädiktiven Parametern orientieren, wobei aktuell in erster Linie (i) der MRT-Befund (Anzahl sowie Lokalisation von Läsionen) ..... zu nennen sind.

Empfehlung 2:

– Für die Einleitung einer DMT bei der schubförmigen MS spricht das Behandlungsziel der Reduktion entzündlicher Aktivität in Form von Erkrankungsschüben und neuen Läsionen in der MRT.

- Als Vorschlag zur Einschätzung einer (hoch-)aktiven schubförmigen MS sollte gelten: ≥1 Schub innerhalb der letzten 12 Monate, ≥2 Schübe in den letzten 24 Monaten oder ≥3 neue T2-L.sionen oder ≥1 neue Gd+-Läsion in einer Verlaufs- MRT (auf die Kontrastmittelgabe kann bei Vorliegen rezenter und qualitativ hochwertiger Verlaufsbilder verzichtet werden) in den letzten 12 Monaten.

6. Welche Arten von Untersuchungen/Parametern sagen bei MS-Patienten unter einer DMT ein schlechtes Ansprechen auf die Behandlung voraus?

Empfehlung 6:

– Ziel der MS-Therapie ist die „bestmögliche“ Krankheitskontrolle und die bestmögliche Lebensqualität des Patienten. Praktisch soll die Krankheitskontrolle gemessen werden anhand klinischer Parameter (v. a. Schübe, Behinderung) sowie MRT-Aktivität (sog. NEDA-Konzept, „no evidence of disease activity“).

DGNeurologie
DOI 10.1007/s42451-021-00353-3

MAGNIMS 2021: MS-Monitoring

Initial	New baseline	First follow-up*†	Second follow-up*†	Follow-ups*†
Pretreatment‡	3–6 months after treatment onset§	12 months after treatment onset	24 months after treatment onset	Every year while on treatment¶
Gadolinium recommended	Gadolinium usually not required‖	Gadolinium optional	Gadolinium optional	Gadolinium optional

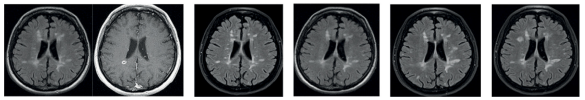


Figure 3: **MRI timing in monitoring of multiple sclerosis**
Images show scans from a single patient over time. *Shorter follow-up MRI (ie, 6 months) if substantial isolated MRI activity or isolated clinical activity. †Add spinal cord MRI to brain MRI if clinically indicated (panel 3). ‡Add spinal cord MRI to brain MRI if never done. §Longer intervals to be considered in patients treated with disease-modifying treatments (eg, up to 9 months with glatiramer acetate and until completion of the full initial course with induction therapies). ¶Less frequent MRI in clinically stable patients treated with interferon beta or glatiramer acetate. ‖Consider gadolinium administration in patients with highly active disease at baseline or in patients with unexpected clinical activity after treatment initiation.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

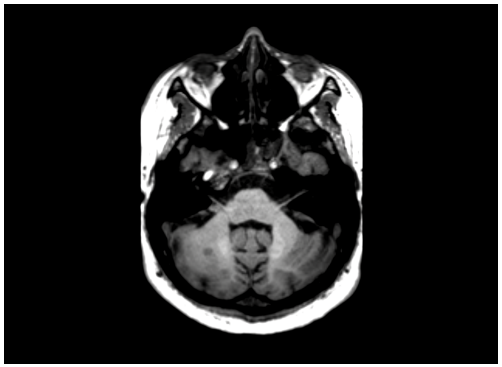
Fall 3, ♀, 39 a

Diagnosen:
hochaktive schubförmige MS (EM und ED 2001) mit Residuen (EDSS 4.5-5.0)

- Ein Schubereignis ist unter Tysabri weiterhin nicht aufgetreten, das Laufen wird aber unsicherer durch eine vermehrte Gangataxie und auch progrediente spastische Paraparese – **Hinweise auf progrediente Elemente**
- 1/2021 erfolgten kraniale und zervikale MRT Kontrollen, die im kurzfristigen Vergleich zu 6/2020 eine stabile Läsionslast belegen
- aber im langfristigen Vergleich der Bilder eine Zunahme der Hirn- und auch Myelonatrophie
- **Aktuell 146. Tysabri-Infusion**

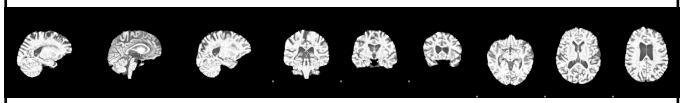
Fall 3, ♀, 39 a
2015, 18 + 21: langfristig stabile Läsionslast

Fall 3, ♀, 39 a
Aber was ist das ? MRTs schon vor 2008 !

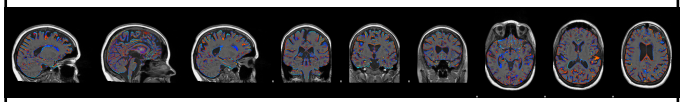


Fall 3, ♀, 39 a
2015-21: Atrophie? Schätzen Sie!

Hirn: PBVC = -3.26 %



Ventrikel: PVVC = +5.36 %



SIENA/VIENA, Teil von FSL; NeuroImage, 17(1):479-489, 2002

MAGNIMS 2021: Standardisierte Befundung

Category	Parameters/findings to report
MRI technique	A brief, concise description of the MRI technique should include: • anatomical area covered (brain, spinal cord, optic nerve) • magnetic field strength • slice thickness • type and dose of GBCA used • type of sequences performed • date and technique of previous scan used for comparison These data are required for proper comparative analysis of examinations that are performed at different time points and at different imaging centres
Findings	This section should start with a comprehensive, systematic description of all the imaging findings related to the specific clinical situation, using standardized terminology. Examples of such findings include: • Lesions: number of T2 lesions* and of Gd-enhancing lesions, topography, size, and shape (with reference to MS characteristics) (on diagnostic scan) • qualitative assessment of T2 and T1 lesion load • semiquantitative visual assessment of brain atrophy • positive and negative imaging features that could be considered as evidence for or against the diagnosis of MS • on follow-up scans, the number of unique active lesions defined as Gd enhancing lesions plus unenhanced new and substantially enlarged T2-hyperintense lesions should be reported (in addition to a brief summary of the points above) • any incidental or unexpected findings, which should be clearly described and interpreted as either clinically relevant or not

GBCA=gadolinium-based contrast agent

* Suggested system for reporting total T2 lesion number: Brain: If <20 lesions, provide exact number; otherwise, report an estimate of "between 20 and 50 lesions," "between 50 and 100 lesions," "more than 100 lesions," or "uncountable (confluent) lesions." Spinal cord: If <10 lesions, provide exact number; otherwise, report "more than 10 lesions" or "diffuse pattern."

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MAGNIMS 2021: Drug-Monitoring *(insbes. PML)*

Panel 5: **Magnetic Resonance Imaging in Multiple Sclerosis-Consortium of Multiple Sclerosis Centres-North American Imaging in Multiple Sclerosis recommendations for the use of MRI for monitoring treatment safety**

General

- Consider opportunistic infections, other medication-related safety events (eg, posterior reversible encephalopathy, acute ischaemic stroke, and haemorrhagic stroke), and even comorbidities that might not be directly related to the specific multiple sclerosis treatment.

Progressive multifocal leukoencephalopathy (PML) screening and detection

- Obtain annual brain MRI according to the standardised acquisition protocol (table 1).
- Do frequent PML screening (ie, every 3–4 months) with an abbreviated MRI protocol (ie, fluid-attenuated inversion recovery, T2-weighted, and diffusion-weighted imaging) exclusively for patients who are treated with natalizumab and have a high risk of PML occurrence (ie, patients who are seropositive for JC virus and have been treated with natalizumab for ≥18 months, with high anti-JC virus antibody index values [>0·9], or previously treated with immunosuppressive therapies). If high-quality 3D fluid-attenuated inversion recovery scans are available, conventional T2-weighted sequences are optional.
- Use gadolinium-based contrast agents to further assess lesions that are suggestive of PML on screening MRI (panel 2).
- Use gadolinium-based contrast agents to detect and monitor PML-immune reconstitution inflammatory syndrome (panel 2).
- Spinal cord MRI is not required for treatment safety monitoring.
- Consider continuous lesion enlargement and typical PML-immune reconstitution inflammatory syndrome on MRI as supportive of PML, even when JC virus DNA is not detected in the CSF.

Potential for carry-over PML

- Do clinical and radiological (ie, brain MRI) baseline evaluation before switching from disease-modifying treatment that is associated with an increased risk of PML.
- Do MRI based pharmacovigilance by use of frequent brain MRI, according to the abbreviated MRI acquisition protocol (table 1), every 3–4 months up to 9–12 months after natalizumab treatment switch in patients at high risk for PML.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

MAGNIMS 2021: Drug-Monitoring *(insbes. PML)*

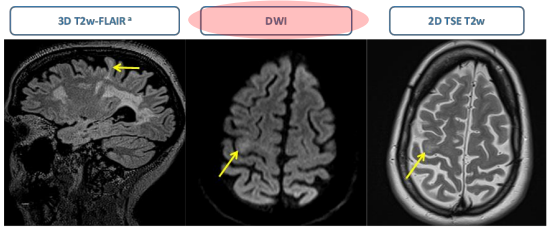


Figure 2. Abbreviated brain MRI protocol for PML screening (observe a small asymptomatic PML lesion in the right pre-Rolandic juxtacortical white matter) (arrows). This abbreviated MRI screening protocol should be performed on a 3-4monthly basis in high risk patients.

Es fehlt KM !

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

Fall 4, ♂, 35 a

Diagnosen:

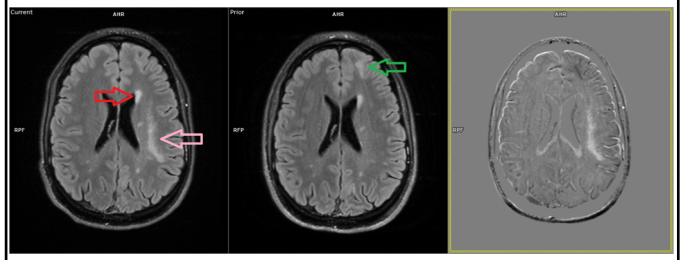
Hochaktive Verlaufsform einer schubförmigen MS

EM 4/2012 – 4 Schübe bis 12/2012 (u.a. mit Sensibilitätsstörungen und Doppelbildern)

- Tysabri-Therapie wurde bereits bei ED 12/2012 während Aufenthalt USA begonnen
- JCV-Antikörper von Anfang an positiv (hoher Index wurde später nachgewiesen)
- Sehr gute Stabilisierung unter Tysabri – **immer schubfrei** – keine neuen Läsionen im MRT
- **Aufweitung des Infusionsintervalls auf 6 Wochen seit 3/2016**
- **81. Infusion am 29.04.2021 mit EDSS 0**

MS-Kontrollen mit Verlaufsdifferenzen
Stärken und Schwächen / Probleme

Fall 4, ♂, 35 a



05/2021 11/2020 Differenz

zusammen mit Thomas Illigen, Siemens Healthcare

How-I-do-it

MAGNETOM Flash (69) 3/2017
www.siemens.com/magnetom-world

FLAIR Fusion in Multiple Sclerosis Follow-up: An Indispensable Tool in Clinical Routine

Stéphane Cantin[1]; Thomas Troalen[2]; Emeline Lamain[1]; Melisa Bakir[2]

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[2] Siemens Healthineers, Saint-Denis, France

Abstract

Multiple sclerosis (MS) follow-up leads to millions of brain MRI scans around the world. Depending on the number and size of inflammatory lesions, comparing successive exams to assess dissemination in time can be a challenging and lengthy process.

This article aims to describe FLAIR image fusion with syngo.via, and to highlight the benefits in terms of new lesion detection capacity and interpretation time saving, compared to conventional frame-by-frame 3D FLAIR comparison.

Equipment

All images were acquired using a 1.5T MAGNETOM Aera system with syngo MR E11 software and the 20-channel head coil. Postprocessing was performed using syngo.via VB10 software.

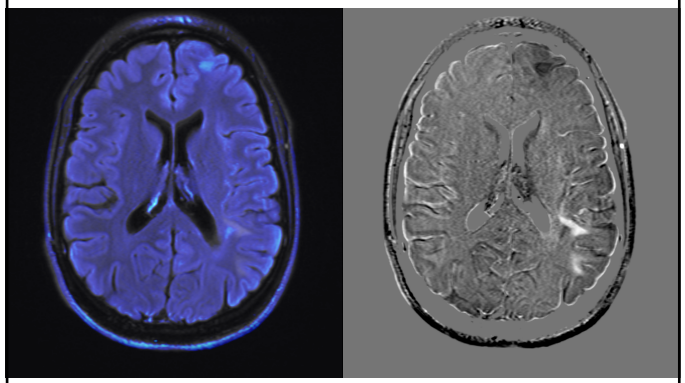
hyperintensities on FLAIR images [3]. In some cases, detecting new lesions can be relatively cumbersome and uncertain.

The common way of identifying new FLAIR hyperintensities is via the frame-by-frame comparison of successive FLAIR sequences. This can be time-consuming, especially with patients who have a high lesion load. Moreover, the comparison is very challenging with coalescing lesions, as subtle increases in size are more difficult to detect than independent new lesions.

According to the literature, the best technique appears to be the subtraction of successive FLAIR sequences [4–5]. However, tools for the co-registration and subtraction of MRI exams acquired at different time points, or even for automatic segmentation are not always available in a clinical environment [6–7].

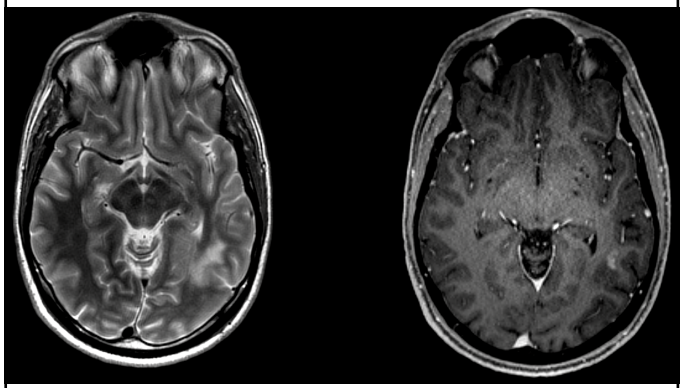
The third technique is FLAIR fusion, which is easily

MS-Kontrollen mit Verlaufsdifferenzen
Farboverlays vs. SW-Subtraktion

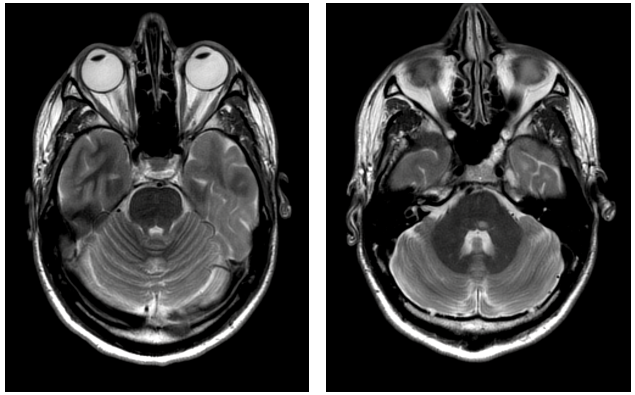


zusammen mit Thomas Illigen, Siemens Healthcare

Die Diagnose ist ? (i)PML !



Nukleärer Abduzenz links !



MAGNIMS 2021: Schwangerschaft, Stillzeit, Kinder

Panel 6: Magnetic Resonance Imaging in Multiple Sclerosis-Consortium of Multiple Sclerosis Centres-North American Imaging in Multiple Sclerosis recommendations for the use of MRI in patients with multiple sclerosis in childhood or during pregnancy and lactation

MRI in paediatric patients with multiple sclerosis

MRI acquisition

- Use the same standardised brain and spinal cord MRI protocols as for adults (tables 1, 2); gadolinium-enhanced images are valuable to exclude non-multiple sclerosis diagnosis at onset but are optional for monitoring purposes (panel 2).
- Full spinal cord MRI should be obtained for diagnosis of children with spinal cord symptoms or signs or with inconclusive brain MRI findings; in other cases, spinal cord MRI could be obtained to provide a baseline MRI; spinal cord MRI is not recommended for regular monitoring, but can be considered if clinically warranted (table 2).
- Dedicated optic nerve MRI is not recommended, except for differential diagnosis with MOG-antibody-associated demyelination or anti-AQP4 antibody disease and if clinical features are atypical (table 1).

Frequency of MRI scanning and assessing imaging measures:

- Use similar scan frequency for monitoring the disease and therapeutic effectiveness as for adults. Increase frequency of imaging (eg, every 6 months) in children with highly active disease or in situations where imaging evidence of treatment benefit aids in advocacy for access to therapies that are approved only for adults with multiple sclerosis.
- Use similar scan frequency for safety monitoring (eg, progressive multifocal leukoencephalopathy screening) as for adults.

MRI measures:

- For detecting MRI activity, reliance on new or enlarging T2 lesions is better than gadolinium-enhancing lesions.
- Brain or spinal cord atrophy and quantitative MRI methods are not recommended for diagnostic and routine clinical monitoring purposes.

MRI during pregnancy

- MRI is not strictly contraindicated during pregnancy; however, the need for MRI during pregnancy should be assessed on a case-by-case basis (eg, clinical presentation that is suggestive of unexpected disease activity or comorbidity, such as cerebral venous thrombosis).
- Use standardised protocols (tables 1, 2) and a magnetic field strength of 1·5 T.
- Gadolinium-based contrast agents during pregnancy are contraindicated (panel 2).
- New or enlarged T2 lesions can be used for detection of disease activity.

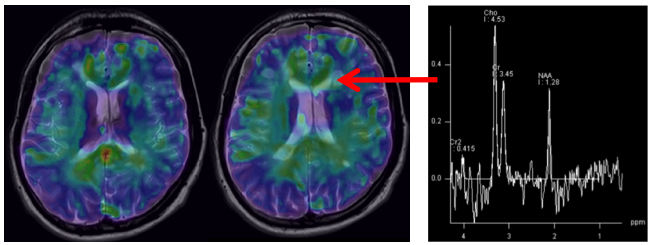
MRI during post partum and lactation

- There is no limitation to use of MRI in the post-partum phase.
- MRI acquisition should be done according to standardised protocols (tables 1, 2).
- The administration of gadolinium-based contrast agents during lactation should be allowed only if highly necessary for diagnostic or monitoring purposes but, if macrocyclic gadolinium-based contrast agents are given, then it might be possible to continue breastfeeding (panel 2).
- Active T2 (ie, new or enlarged) lesions are the preferred measure for inflammatory disease activity.
- A new baseline brain MRI after pregnancy (ie, 2–3 months post partum) is recommended.

The Lancet Neurology DOI: (10.1016/S1474-4422(21)00095-8)

Ausblick:

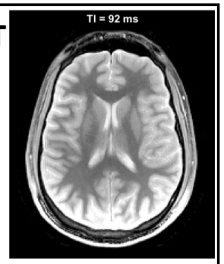
Warum eigentlich Multiple *Sklerose*?
Was ist mit Spektro?
Was ist „hip“, was setzt sich durch?

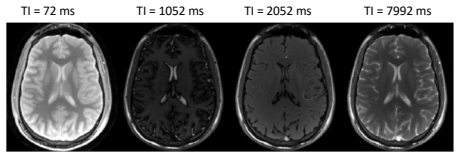


MR-Elastographie (TREMR) Stiffness Map auf T2-TSE (Overlay)

Ausblick: "1-Stop-Shop-All" MRT

- 3T Siemens Skyra
- 20-channel head coil
- PCA based reconstruction [1]
- Resolution: 1 x 1 x 4 mm³
- TR = 4.0 ms, **2000 Echoes**
  - ➔ ~400 reconstructed images





[1] Pfister J, et al. *Magn Reson Med.* **2019**;81(6):3488-3502

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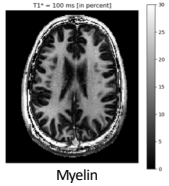
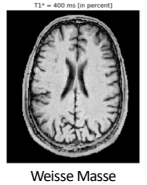
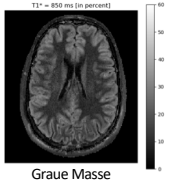
Ausblick: Quantitative Gewebekarten



Myelin



Weisse Masse

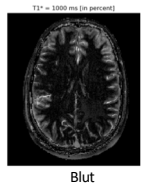


Graue Masse

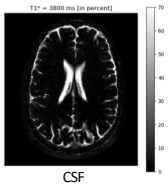
2D Multishot Measurement

(Proof-of-principle):

- TA = 2:30 min
- Resolution = 1 x 1 x 4 mm³



Blut



CSF

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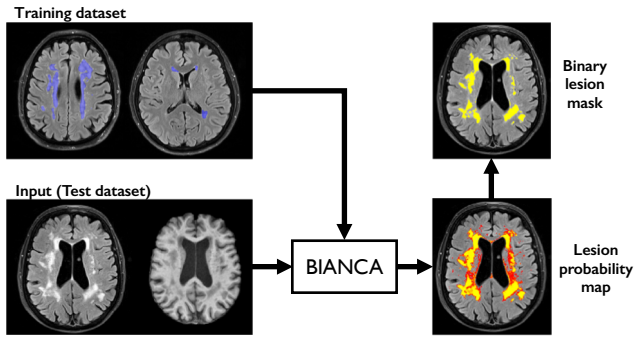
Ausblick: ML/KI-basierte Läsionsdetektion

Brain Intensity AbNormalities Classification Algorithm (BIANCA)



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Griffanti et al., NeuroImage 2016

Danke für Ihre Zeit und Aufmerksamkeit!