

Corso FAD ECM

INNI –

SCLEROSI MULTIPLA

Gemelli



SCLE^{ONUS}
ROSI
MULT
IPLA
fondazione
italiana

un mondo
libero dalla SM

Provider ECM n. 5599

The Italian Neuroimaging Network Initiative (INNI)

Formazione
per l'eccellenza

apr. '23

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore





This work is licensed under a Creative Commons Attribution 4.0 International License.

TSRM Ada Guidi - Marino Gentile
Radiographer

Gemelli

✉ marino.gentile@outlook.com

✉ www.variodyne.it

apr. '23

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore





THE ITALIAN NEUROIMAGING
NETWORK INITIATIVE (INNI)

*Verso la standardizzazione dell'utilizzo della
RM nel paziente con Sclerosi Multipla a
livello nazionale*



Gemelli



**The Italian Neuroimaging Network Initiative (INNI):
verso la standardizzazione dell'utilizzo della RM nel paziente
con Sclerosi Multipla a livello nazionale**

apr. '23

SCUOLA ASSOCIATIVA

AIMS

CORSI ECM

FISM

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore





THE ITALIAN NEUROIMAGING NETWORK INITIATIVE (INNI)

Verso la standardizzazione dell'utilizzo della RM nel paziente con Sclerosi Multipla a livello nazionale

Gennaio - Novembre 2023

INTRODUZIONE

M.A. Battaglia, M. Filippi

LINEE GUIDA PER L'ACQUISIZIONE E LA REFERTAZIONE DELLA RM NEL PAZIENTE CON SM

P. Pantano

VERSO LA STANDARDIZZAZIONE DELLA VALUTAZIONE DELLE LESIONI DELLA SOSTANZA BIANCA NEL PAZIENTE CON SM

M. A. Rocca

VERSO UNA STANDARDIZZAZIONE PER LA MISURAZIONE DELL'ATROFIA NEL PAZIENTE CON SM

N. De Stefano

COLLABORAZIONE CON IL REGISTRO SM: CONDIVISIONE DELLA SURVEY CONOSCITIVA

A. Gallo

DISCUSSIONE

M. Filippi, M. Trojano

SCUOLA ASSOCIATIVA
AIMS

CORSI ECM
FISM

<https://www.aims.it/>

<https://fad.aims.it/login/?lang=it>

SCLE ONLUS
ROSI
MULT
IPLA
fondazione
italiana

un mondo
libero dalla SM

Provider ECM n. 5599

Il **data base INNI** - www.inni-ms.org/ - raccoglie oggi i dati di risonanza magnetica di un certo numero di Centri Clinici SM che hanno già aderito al progetto. I dati comprendono non solo esami di risonanza magnetica, ma anche le informazioni demografiche, cliniche e neuropsicologiche. Dal 2014 i progetti di ricerca INNI hanno contribuito a sviluppare nuovi protocolli di risonanza magnetica e metodologie appropriate per la gestione dei dati multicentrici nella SM, in particolare per quanto riguarda l'acquisizione ed elaborazione di immagini relative alla valutazione delle lesioni della sostanza bianca e dell'atrofia. Parametri quest'ultimi strumentali alla diagnosi e al monitoraggio della progressione della malattia.

INNI – Sclerosi Multipla



DATI EPIDEMIOLOGICI E RICERCHE SPECIFICHE PER VALUTARE L'IMPATTO DELL'INFEZIONE COVID-19 NELLE PERSONE CON SM IN TRATTAMENTO CON TERAPIE MODIFICANTI LA MALATTIA, E ORA CON I VACCINI



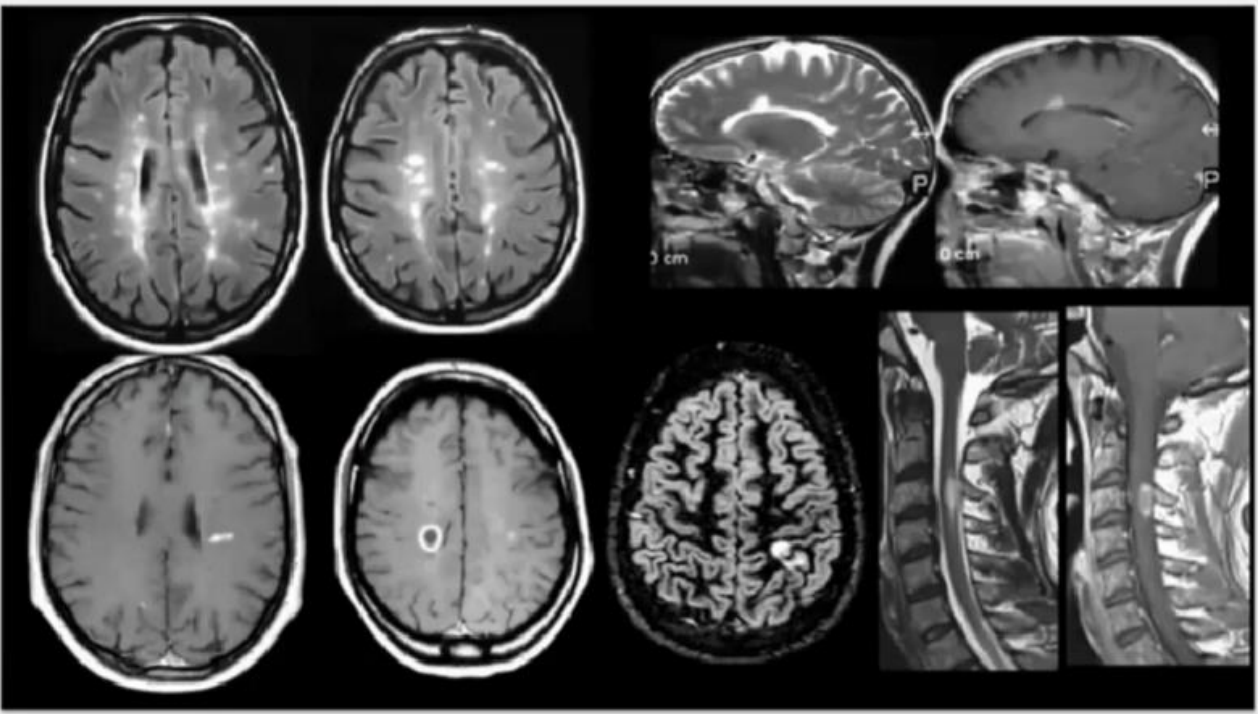
REGISTRO ITALIANO SM

<https://registroitalianosm.it/index.php>



INNI – Sclerosi Multipla

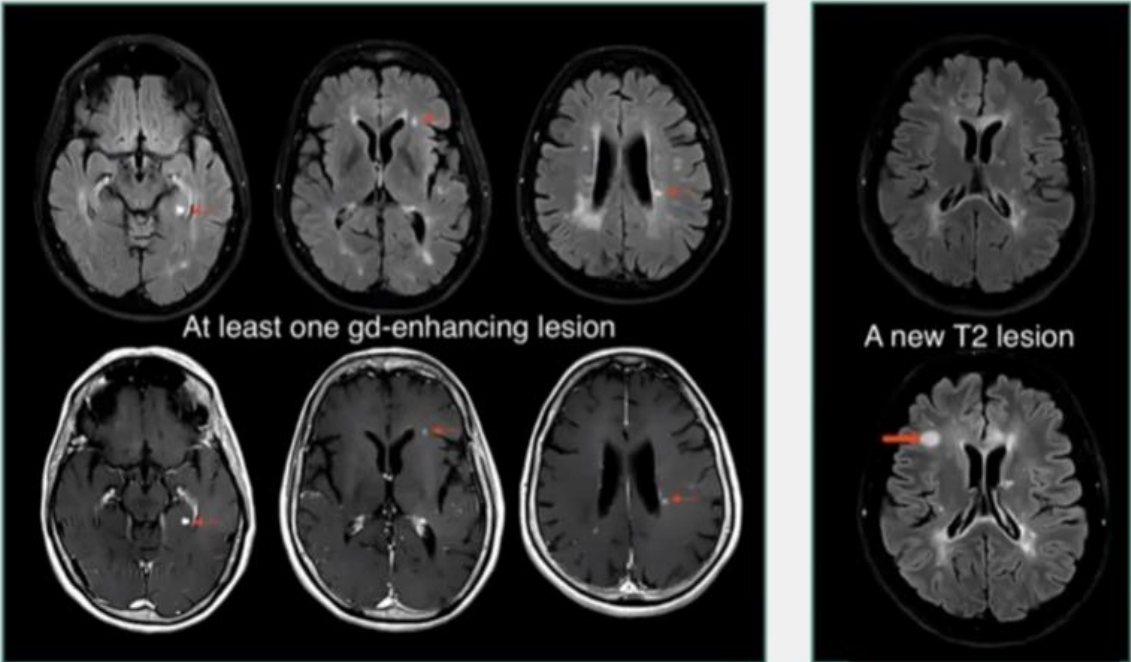
La RM ha completamente rivoluzionato l'approccio al paziente con SM in termini di diagnosi, prognosi e monitoraggio del trattamento



INNI – Sclerosi Multipla

Diagnostic Criteria

Dissemination in time. The development or appearance of new CNS lesions over time.



INNI – Sclerosi Multipla

The screenshot shows the INNI website interface. At the top, there is a navigation bar with 'Home', 'Project', 'News', 'Documents', and 'Login'. Below this is the 'Advanced MRI' section, which displays various brain scan results. On the left, there are two sets of brain surface renderings labeled 'fMRI'. In the center, there are three axial slices of a brain scan labeled 'DTI'. To the right of the DTI slices, there are three more axial slices labeled 'T1-3D'. At the bottom of the screenshot, there is a row of logos for the participating institutions: COSEI OPERATORI, CENTRO SAN RAFFAELE, Ospedale San Raffaele, UNIVERSITA DI SIENA, V: Università degli Studi della Campania Luigi Vanvitelli, Dipartimento di Scienze Mediche e Chirurgiche, SAPIENZA Università di Roma, and SCLE ROSI MULTIPLA Fondazione Italiana.

Diagnostic Criteria

Dissemination in space. At least two MRI lesions in specific CNS locations.

- **Cortical MRI lesions**
- **Juxtacortical MRI lesions**
- **Periventricular MRI lesions**
- **Infratentorial MRI lesions**
- **Spinal cord MRI lesions**

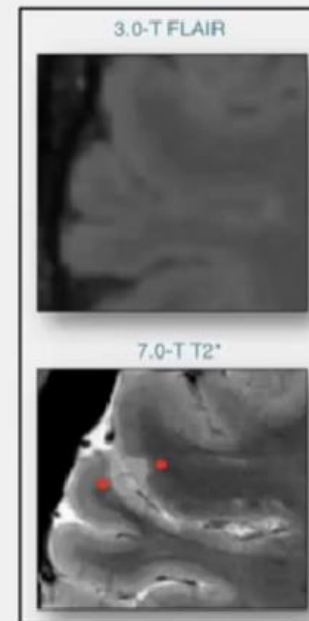
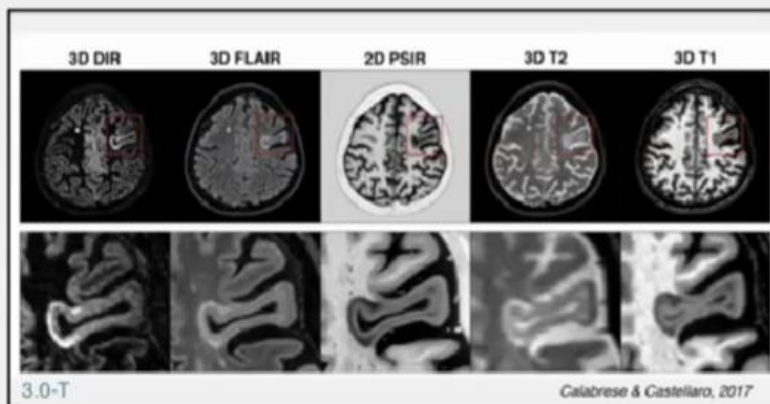


INNI – Sclerosi Multipla

Cortical MRI lesions

Lesions seen with special MRI techniques* within the cerebral cortex (leukocortical, purely intracortical or subpial lesions)

DIR, PSIR, T2, T1

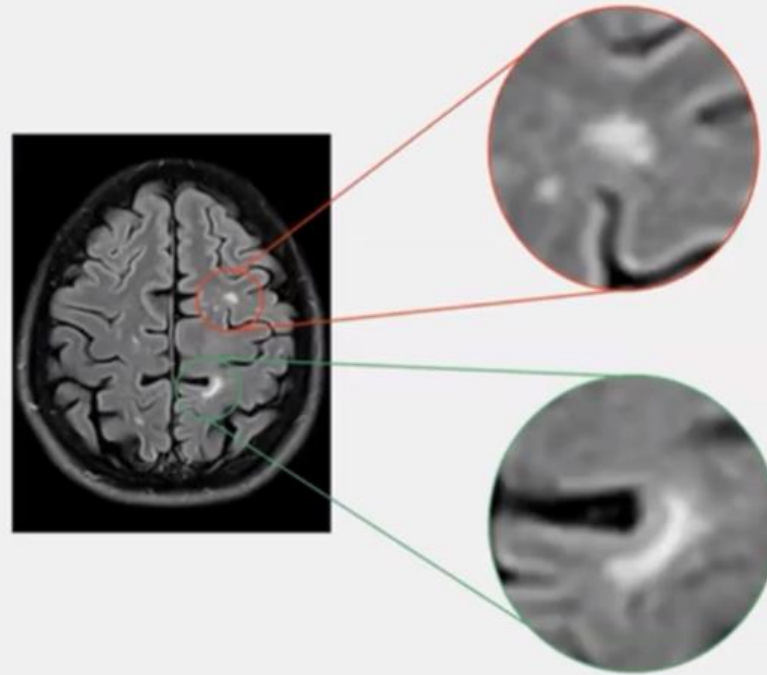


Courtesy of Dr. C. Mainero, MGH



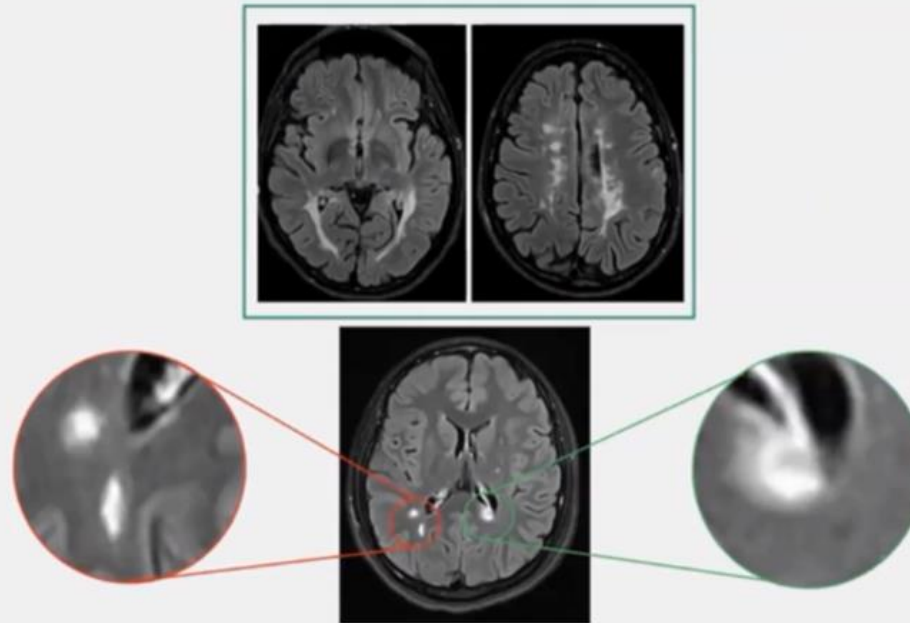
Juxtacortical MRI lesions

T2-w hypointense white matter lesions abutting the cortex, and not separated from it by white matter



Periventricular MRI lesions

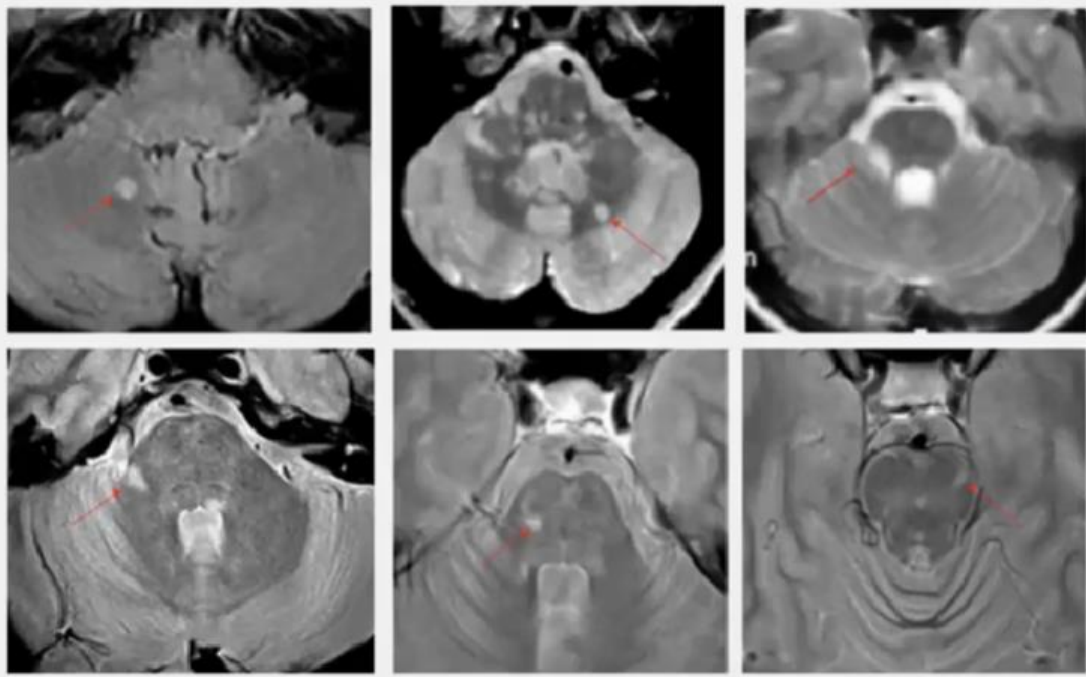
T2-w hypeintense white matter lesions abutting the lateral ventricles without white matter in between, including lesions in the corpus callosum but excluding lesions in deep grey matter structures



INNI – Sclerosi Multipla

Infratentorial MRI lesions

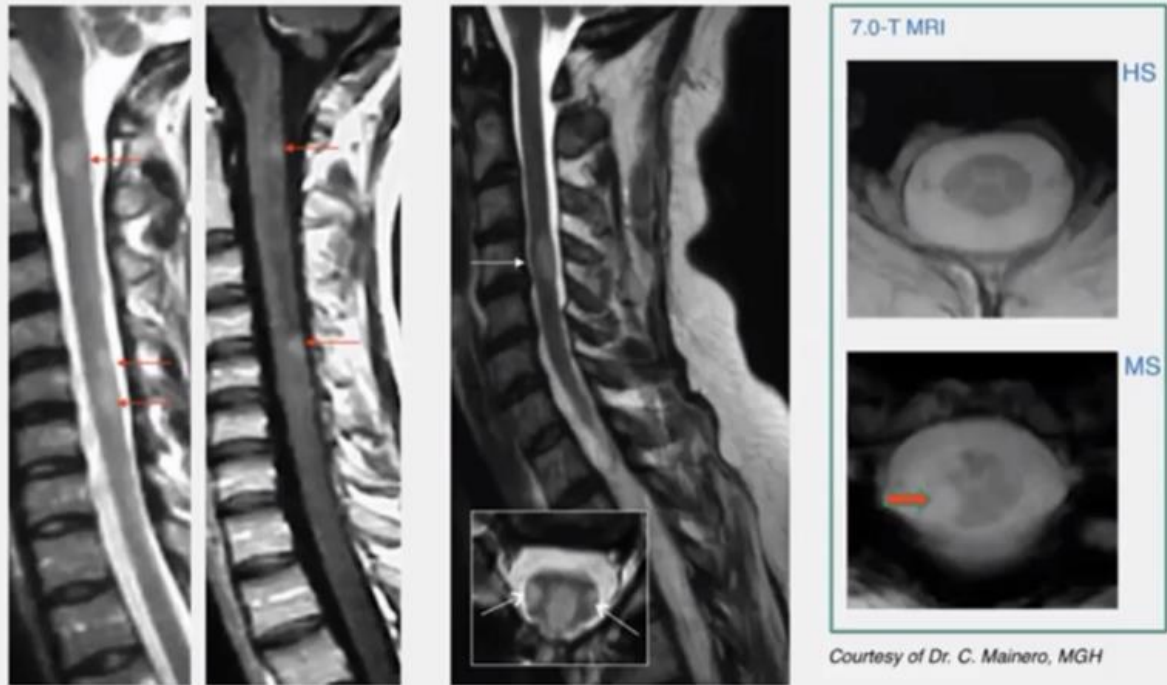
T2-w hypointense lesions in the brainstem, cerebellar peduncles, or cerebellum



INNI – Sclerosi Multipla

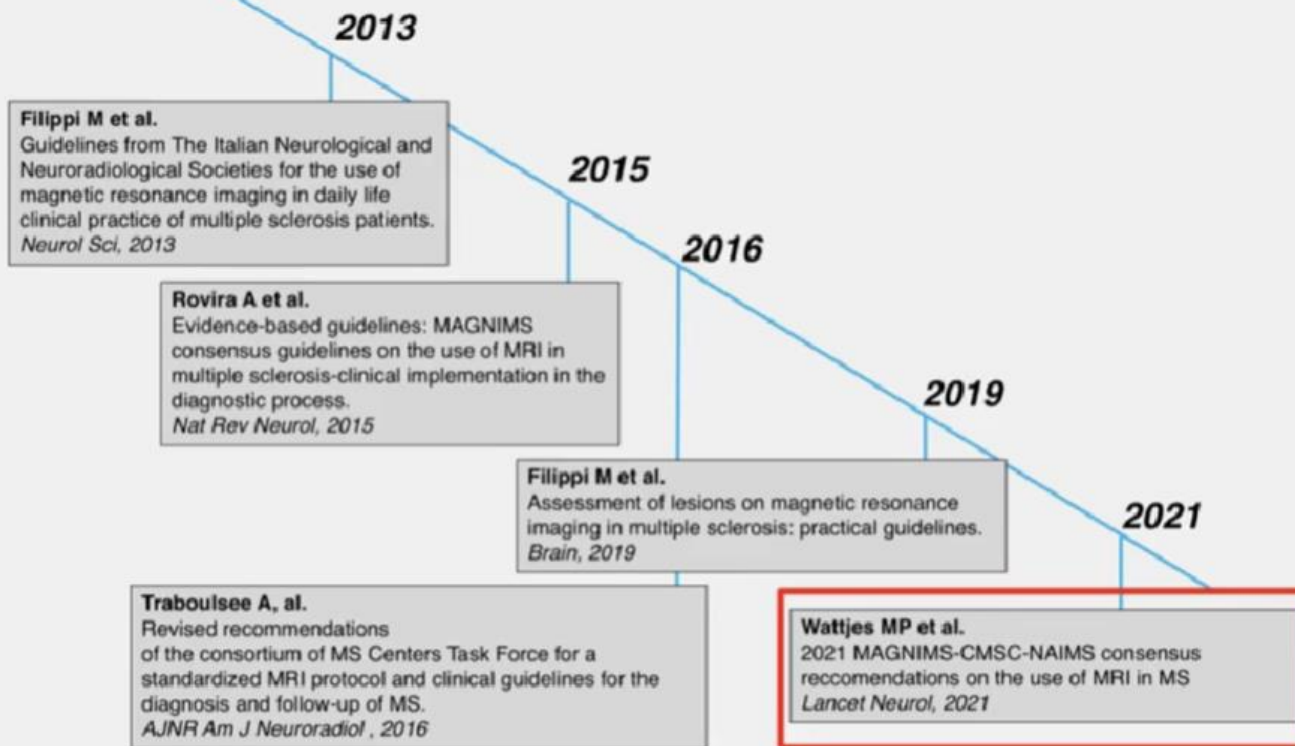
Spinal cord MRI lesions

Hyperintense lesions in the spinal cord seen on T2 plus short tau inversion recovery, proton-density images, or other appropriate sequences, or in two planes on T2 images



INNI – Sclerosi Multipla

Linee guida per l'uso della RM



Linee guida per l'uso della RM

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, Claudio 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**

Lancet Neurol 2021; 20: 653–70

Published Online

June 14, 2021

[https://doi.org/10.1016/S1474-4422\(21\)00095-8](https://doi.org/10.1016/S1474-4422(21)00095-8)



Linee guida per l'uso della RM

Protocollo standardizzato Encefalo
Protocollo standardizzato Midollo

1 **Basale:
Diagnosi di SM**

2 **Follow-up:
Monitoraggio**

Attività di malattia

Efficacia del Trattamento

Complicanze del Trattamento



Linee guida per l'uso della RM

1

Basale: Diagnosi di SM

BRAIN

Field strength	≥1.5 T (preferably 3 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)
In-plane resolution	≤1 mm × 1 mm
Coverage	Whole brain (include as much of cervical cord as possible)
Axial scan orientation	Subcallosal plane to prescribe (ie, for 2D imaging) or reformat (ie, for 3D imaging) axial oblique slices

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



Linee guida per l'uso della RM

SPINAL CORD

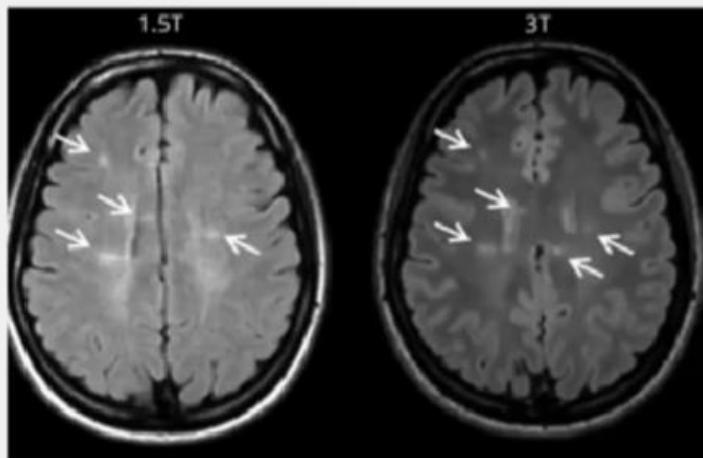
Field strength	≥ 1.5 T (3 T has no added value compared with 1.5 T)
Slice thickness	Sagittal slices should be ≤ 3 mm with no gap; axial slices should be ≤ 5 mm with no gap
In-plane resolution	≤ 1 mm \times 1 mm
Coverage	Cervical and thoracolumbar spinal cord, to include conus
Axial scan orientation	Perpendicular to the sagittal axis of the spinal cord



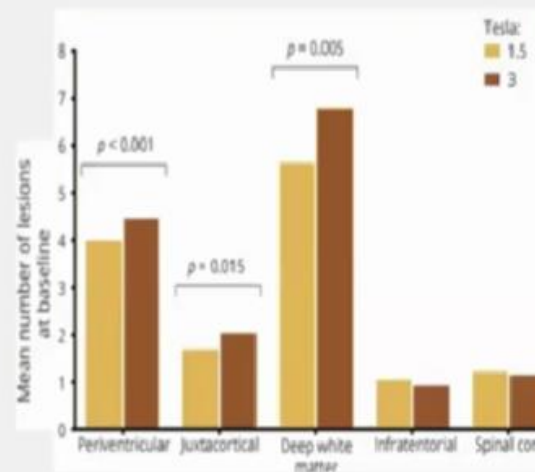
Linee guida per l'uso della RM

Diagnosi di SM

Three-Tesla MRI does not improve the diagnosis of multiple sclerosis. A multicenter study



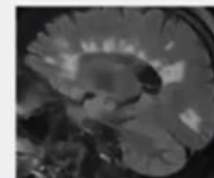
66 patients with CIS within 6 months from symptom onset collected in 6 MRI European centers



MAGNIMS, Neurology 2018

Linee guida per l'uso della RM

Diagnosi di SM



Brain MRI protocol

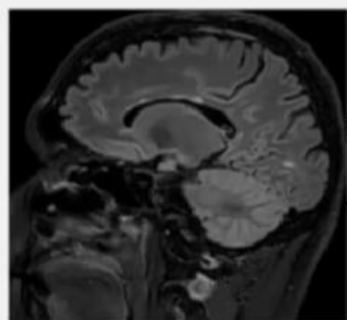
Axial T2-weighted (TSE or FSE) sequences†	Recommended
Sagittal T2-weighted FLAIR (preferably 3D; fat suppression is optional)	Recommended
Axial T2-weighted FLAIR (unnecessary if a sagittal 3D FLAIR with multiplanar reconstruction is obtained; fat suppression is optional)	Recommended
Axial (or 3D sagittal) T1-weighted sequences after contrast‡	Recommended
Diffusion-weighted imaging	Optional
Double inversion recovery or PSIR for detecting cortical or juxtacortical lesions	Optional
High-resolution T1-weighted sequences (isotropic 3D acquisition; for quantitative assessment of brain volume)	Optional
Susceptibility-weighted imaging	Optional for assessing the central vein sign



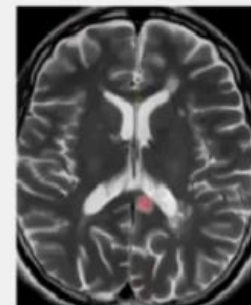
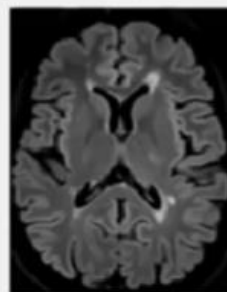
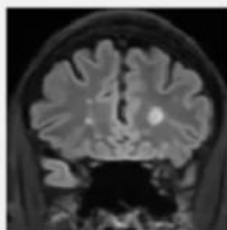
Linee guida per l'uso della RM

Diagnosi di SM

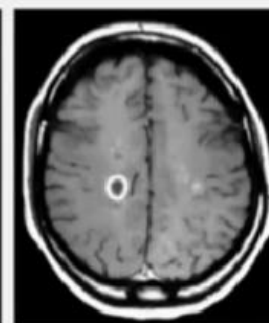
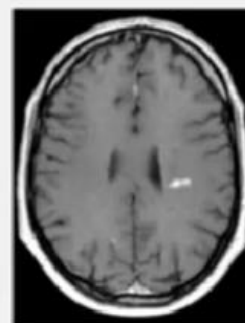
Sequenze raccomandate



3D FLAIR



Assiale T2 TSE



Assiale T1 post mdc

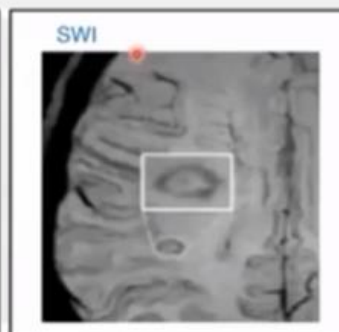
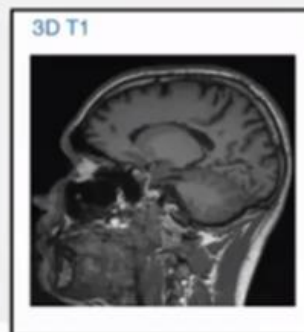
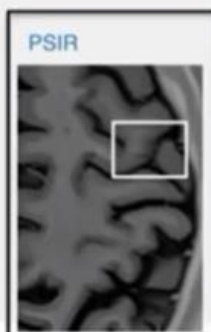


Linee guida per l'uso della RM

Diagnosi di SM

Sequenze facoltative

Diffusion-weighted imaging	Optional	→ PML
Double inversion recovery or PSIR for detecting cortical or juxtacortical lesions	Optional	→ Lesioni corticali
High-resolution T1-weighted sequences (isotropic 3D acquisition; for quantitative assessment of brain volume)	Optional	→ Volumetria
Susceptibility-weighted imaging	Optional	→ Vena centrale, iron ring



Linee guida per l'uso della RM

Diagnosi di SM

RM ENCEFALO

In sintesi:



- Campo magnetico $\geq 1.5T$ (preferibile 3T)
- Sezione $\leq 3mm$ (3D imaging preferibile)
- Protocollo di acquisizione e posizionamento della testa standardizzati
- Dose singola di gadolinio (0.1 mmol/kg pc) con ritardo di 5 min tra iniezione e acquisizione



Linee guida per l'uso della RM

Diagnosi di SM

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 
Sagittal 3D heavily T1-weighted sequences (PSIR or magnetisation-prepared rapid acquisition of gradient echoes) only for the cervical segment	Optional
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
Sagittal T1-weighted sequences (TSE or FSE) before contrast	Optional
Sagittal T1-weighted sequences (TSE or FSE) after contrast‡	Recommended 
Axial T1-weighted sequences (TSE or FSE) after contrast‡	Optional

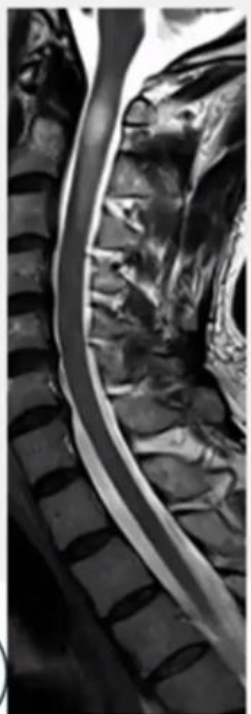


Linee guida per l'uso della RM

Diagnosi di SM

SPINAL CORD

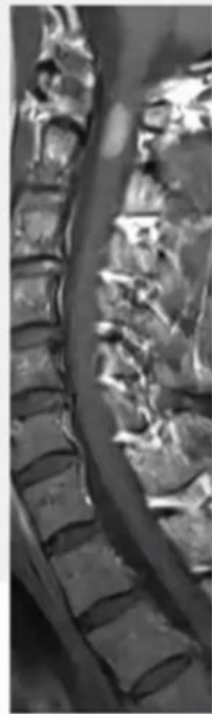
T2 TSE



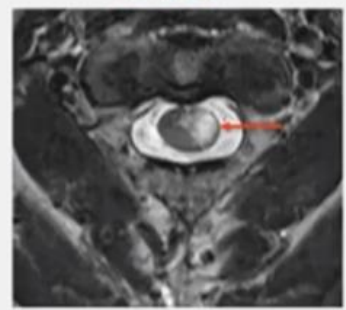
T2 STIR



T1 gd



T2 TSE



Linee guida per l'uso della RM

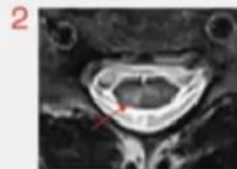
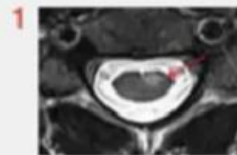
Diagnosi di SM

SPINAL CORD

T2 TSE



T2 STIR



Linee guida per l'uso della RM

Diagnosi di SM

RM MIDOLLO SPINALE

In sintesi:

- Campo magnetico $\geq 1.5T$
- Sezione $\leq 3mm$ sul piano sagittale
- Protocollo di acquisizione standardizzato con almeno due sequenze T2 sul piano sagittale
- Direttamente dopo somm.ne di dose singola di gadolinio



INNI – Sclerosi Multipla

Linee guida per l'uso della RM

Protocollo standardizzato Encefalo
Protocollo standardizzato Midollo

1 **Basale:
Diagnosi di SM**

2 **Follow-up:
Monitoraggio**

Attività di malattia

Efficacia del Trattamento

Complicanze del Trattamento

In generale:

- Stesso posizionamento
- Stesso protocollo (semplificato)
- Midollo non sempre necessario
- MDC non sempre necessario

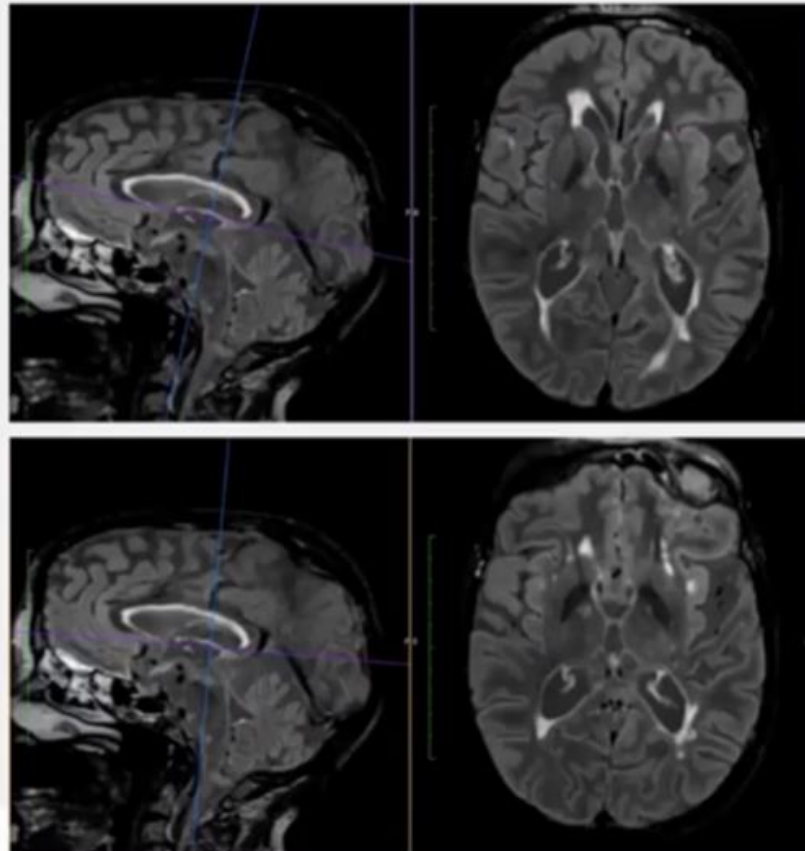


Linee guida per l'uso della RM

Follow-up: Monitoraggio

Posizionamento
Ricostruzione immagini 3D

Linea bicallosale



Diversa ricostruzione dello stesso esame

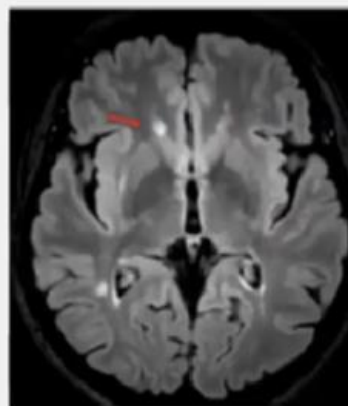
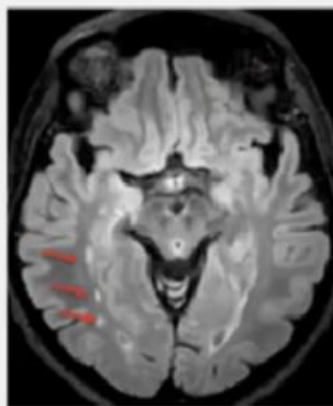
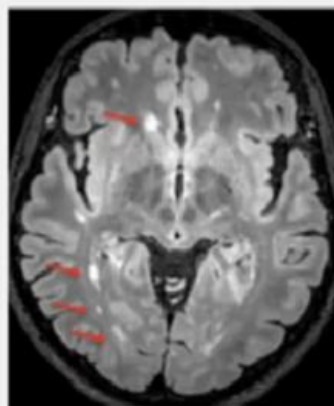


Linee guida per l'uso della RM

**Follow-up:
Monitoraggio**

Riposizionamento non corretto

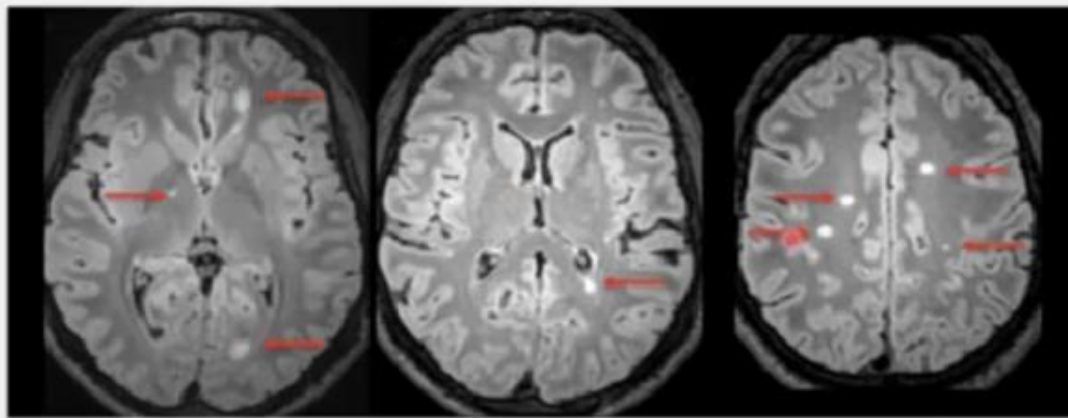
Esame precedente



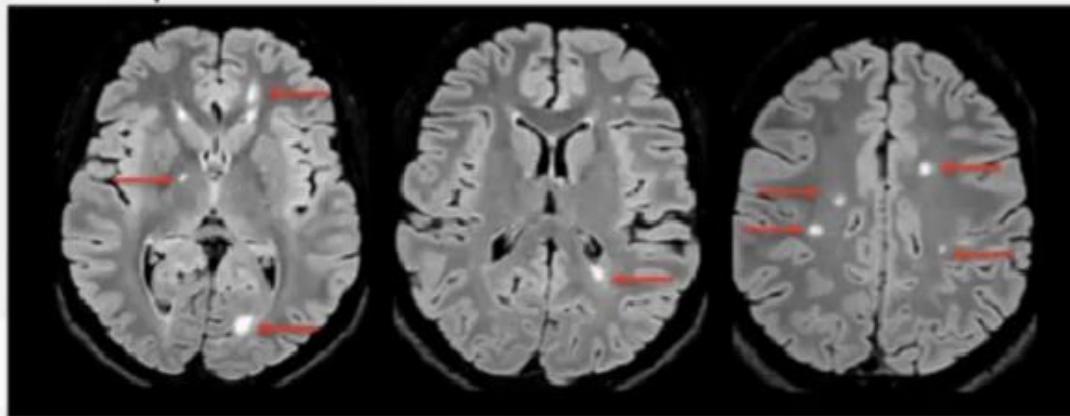
Linee guida per l'uso della RM

**Follow-up:
Monitoraggio**

Riposizionamento corretto



Esame precedente

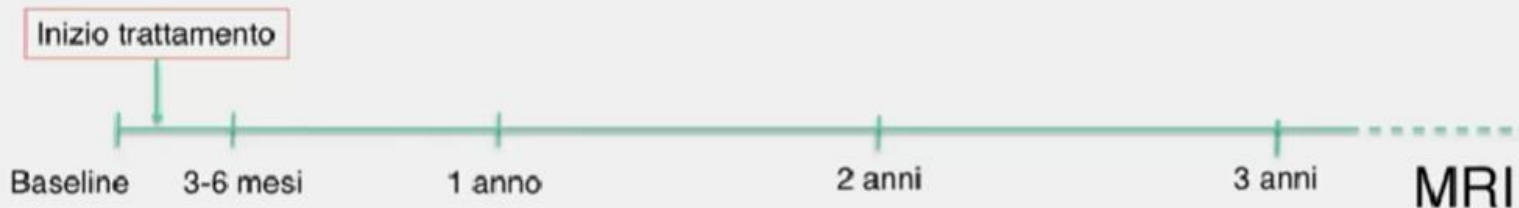


INNI – Sclerosi Multipla

Linee guida per l'uso della RM

**Follow-up:
Monitoraggio**

Efficacia del Trattamento



- Protocollo MRI abbreviato (3D-FLAIR + T1 (non sempre necessario post-MDC)
- Se attività MRI (non clinica) follow-up ogni 6 mesi
- Midollo non sempre necessario



Linee guida per l'uso della RM

Follow-up: Monitoraggio

Complicanze del Trattamento

Progressive multifocal leukoencephalopathy (PML)

T2w e FLAIR

Area iperintensa, con coinvolgimento fibre a U, bordi sfumati verso la corteccia, circondata da lesioni puntiformi (milk way)

Senza edema o effetto massa

T1w

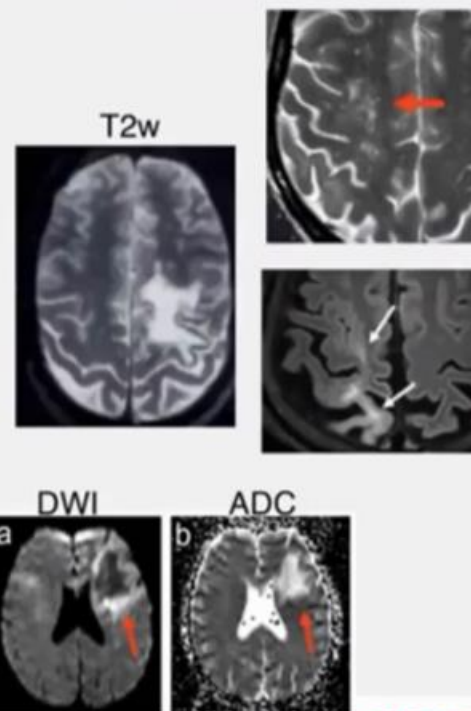
iso- o ipointensa

T1 (Gd)

Generalmente NO CE (DD con IRIS)

ADC/DWI

Restrizione ai bordi della lesione



Il referto radiologico

TECNICA:

Magnete (1.5 vs 3T), elenco sequenze, mdc (tipo e dose).

INDICAZIONI CLINICHE:

Sintomatologia (ricidiva?), fenotipo, disabilità, trattamento.
Quesito specifico?

REPERTI:

- Lesioni (T2 e T1gd): numero, dimensioni, forma, sede.
- Valutazione qualitativa o semiquantitativa dell'atrofia cerebrale e/o midollare.
- Follow-up: nuove lesioni T2 e T1gd: numero, dimensioni, forma, sede.
- Altri reperti.

CONCLUSIONI:

Diagnosi: criteri diagnostici DIS e DIT; attività di malattia; interpretazione radiologica in rapporto al questo clinico; eventuale diagnosi differenziale.

Follow-up: attività di malattia; stabilità o progressione; possibili complicanze (es. PML).





Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

M.A. Rocca

Neurology Unit and Neuroimaging of CNS White Matter Unit,
Division of Neuroscience, San Raffaele Scientific Institute,
Vita-Salute San Raffaele University, Milan, Italy



Outline

- **The INNI initiative / MRI protocol**
- **The INNI initiative / Lesion assessment**
- **The INNI initiative / Quality control**
- **New automatic approaches for lesion identification and quantification**
- **Conclusions**



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



The INNI initiative

- Conventional MR sequences (dual-echo, FLAIR and T1- weighted imaging) provide important pieces of information for diagnosing MS, understanding its natural history and assessing treatment efficacy
- Standardization of MR protocols/procedures outside the setting of clinical trials is still lacking
- The first two goals of the Italian Neuroimaging Network Initiative (INNI) were:
 1. **The creation of a web-based system** with clinical, neuropsychological and MRI data from the participating centers, to allow data sharing
 2. **The use of such data to perform large-scale studies** to define the role of clinical, neuropsychological and advanced MRI biomarkers in understanding MS pathophysiology

The INNI initiative will help to define standardized MRI and clinical protocols for the evaluation of patients with MS at a national level



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



Gemelli



un mondo libero dalla SM



apr. '23

INNI – Sclerosi Multipla

The INNI initiative

Neurol Sci (2017) 38:1029–1038
DOI 10.1007/s10072-017-2903-z



ORIGINAL ARTICLE

The Italian Neuroimaging Network Initiative (INNI): enabling the use of advanced MRI techniques in patients with MS

M. Filippi^{1,2} · G. Tedeschi^{3,4} · P. Pantano^{5,6} · N. De Stefano⁷ · P. Zoratti⁸ · M. A. Rocca^{1,2} · For the INNI Network

Available at: <https://data.base.inni-ms.org>

Sites	Patients	Data
Current number of sites: 4	Current number of patients: 1773	Current number of MRI exams: 3121

4561 MRI exams uploaded

Financially supported by a research Grant from Fondazione Italiana Sclerosi Multipla (FISM 2013/S/1)



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



apr. '23



INNI – Sclerosi Multipla

The INNI initiative User interfaces

MRI exam

[Edit](#) [Delete](#)

Exam date	10/10/2012
Patient age at exam	34
Hash	28ef8246-88343f9b-497a5ef7-1af56a26-a2d91ea4
Study description	FMRI
Scanner	PHILIPS-AD4051C Philips Medical Systems

Study series

[Upload DICOM files](#)

Serie type	Serie description	Note	Serie ID
3D T1	T1W/3DVOL/T		2345e57c-dabe112a-881
DTI	dti35-reg		a5e2a3bb-b794bfde-758
DIR	eiDIR		44467b3a-21200ead-da
Resting State	RESTING		9a0b8d15-43f03cda-3aa
Dual Echo	DUAL_TSE_newFORTE		f7b233bb-a0657016-cf2f

[Edit series from DICOM server](#)

© Consortium GARR 2015



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



IST
ITALS
Newsweek
LEITALIA
statista

The INNI initiative / MRI protocol

Minimum requirement of the MRI protocol to be uploaded on INNI:

1. Sequences for **lesion quantification**: **dual echo** (DE) or **T2-weighted/FLAIR** scans acquired with axial orientation and a slice thickness of no more than 3 mm
2. Sequences for **atrophy quantification**: high-resolution **3D T1-weighted** scans
3. **DT MRI** sequences acquired with *30 diffusion-weighted direction and a nearly isotropic spatial resolution
4. **RS fMRI** sequences covering all brain, with at least 140 scans and an acquisition session at least 5 min long

All sequences **should** be acquired on a **3T MR** scanner

Filippi et al., Neurol Sci 2017



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



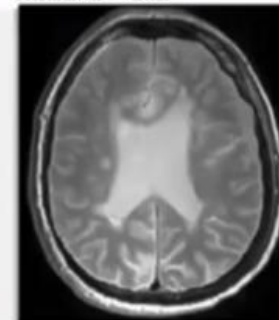
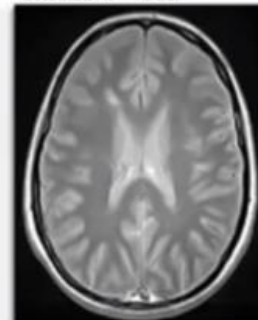
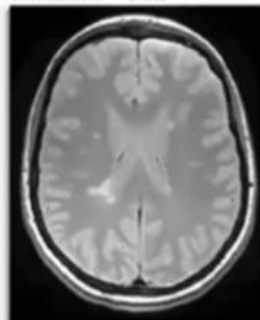
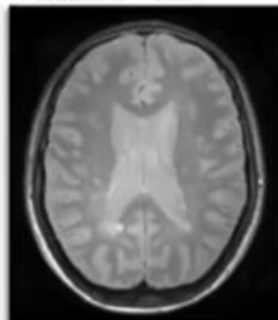
INNI – Sclerosi Multipla

The INNI initiative / MRI protocol

MRI parameters of the sequences used **for lesion assessment** included at the time of the creation of the INNI database by each promoting center

Filippi et al., Neurol Sci 2017

Sequence	Milan	Naples	Rome	Siena
Coil	8 channel head coil	8 channel head coil	12 channel head coil	32 channel head coil
<u>Dual echo</u>	TR = range 2599–2910 ms	TR = 3080 ms	TR = range 3320–5310 ms	TR = 4000 ms
	TE = 16/80 ms	TE = 24/127.5 ms	TE = 10/103 ms	TE = 15/100 ms
	FA = 90°	FA = 90°	FA = 150°	FA = 90°
	Matrix = 256 × 256	Matrix = 256 × 384	Matrix = 384 × 384	Matrix = 240 × 240 (recon 352 × 352)
	FOV = 240 × 240 mm	FOV = 240 × 240 mm	FOV = 220 × 220 mm	FOV = 240 × 240 mm
	Thickness = 3 mm	Thickness = 3 mm	Thickness = range 3 mm	Thickness = 3 mm
	No. of slices = range 44–50	No. of slices = 44	No. of slices = range 45	No. of slices = 44
	Orientation = axial	Orientation = axial	Orientation = axial	Orientation = axial



Prospectively evolving...



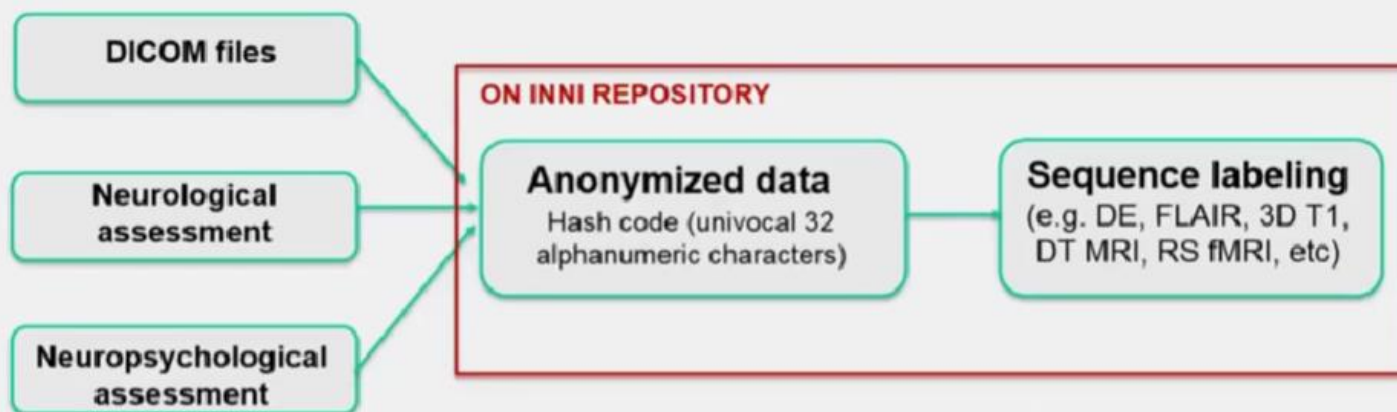
Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



un mondo libero dalla SM

INNI – Sclerosi Multipla

The INNI initiative / Collecting data



- **No identifying patients' information** is stored in the INNI platform
- Patient data are assigned to a **unique identification code** (ID), one-way function
- To ensure subjects' privacy, **any personal information is deleted** from DICOM files
- The database content is available **for authorized users only**



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



Outline

- The INNI initiative / MRI protocol
- **The INNI initiative / Lesion assessment**
- The INNI initiative / Quality control
- New automatic approaches for lesion identification and quantification
- Conclusions



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

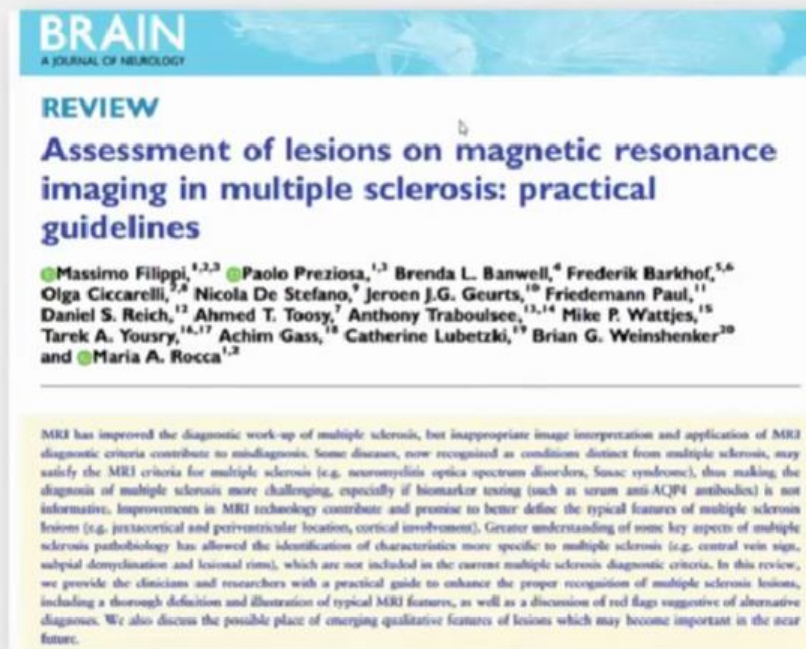


un mondo libero dalla SM



The INNI initiative / Lesion assessment

Practical standardize guidelines for brain T2-hyperintense lesion identification applied to INNI data



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



T2-hyperintense lesions

- Focal hyperintensity on a T2-w (T2, T2-FLAIR or similar) or a proton density (PD)-w sequence
- **Round to ovoid** in shape, ranging from a few millimeters to more than one or two centimeters in diameter. Generally, **≥3 mm** in their long axis
- Lesions should be visible on at least **2 subsequent slices** to exclude artifacts or small hyperintensities, although in acquisitions with higher slice thickness (e.g., ≥ 3 millimetres), smaller lesions could be visible on a single slice
- Asymmetrically distributed mainly in the early stages
- Lesions can occur in any CNS region, with a predilection of specific WM regions (periventricular and juxtacortical WM, corpus callosum, infratentorial areas and spinal cord)

Filippi et al., Brain 2019



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

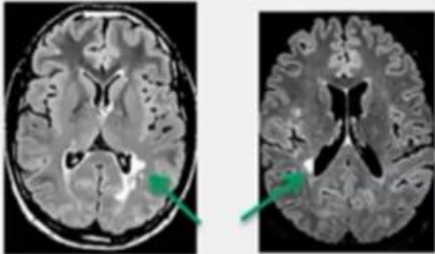
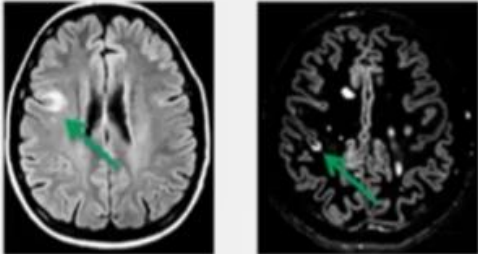
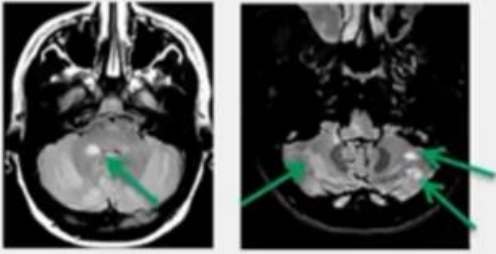
**SCLE
ROSI
MULTI
IPLA**
fondazione
italiana
un mondo
libero dalla SM

2022
Newsweek
statista

INNI – Sclerosi Multipla

The INNI initiative / Lesion assessment

Filippi et al., Brain 2019

Lesion category	Green flags
 <p>Periventricular</p>	<p>Location: abutting the lateral ventricles without intervening white matter</p>
 <p>Juxtacortical/ Cortical</p>	<p>Location: touching or within the cortex</p>
 <p>Infratentorial</p>	<p>Location: brainstem, cerebellar peduncles and cerebellar hemispheres; contiguous to cisterns or the floor of the fourth ventricle; surface of the pons and the pontine trigeminal root entry zone; lining of CSF border zones; cerebral peduncles and close to the periaqueductal gray matter; uni- or bilateral paramedian location in medulla oblongata</p>



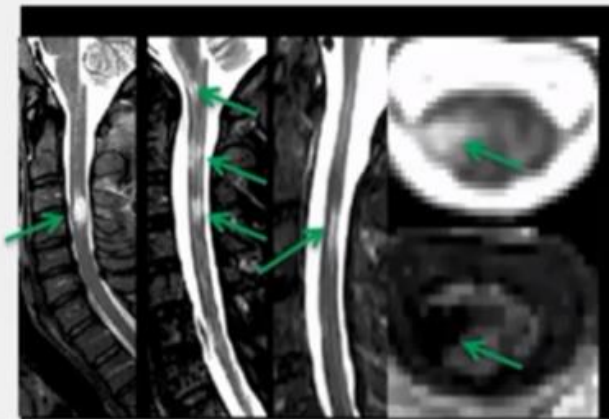
Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

**SCLE
ROSI
MULT
IPLA**
fondazione
italiana
un mondo
libero dalla SM

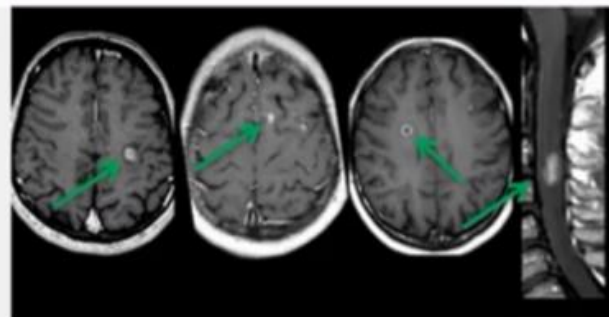
2022
ALS Newsweek
TALIA statista
VERISTARIO A. GENELLI

The INNI initiative / Lesion assessment

Filippi et al., Brain 2019



Lesion category	Green flags
Spinal cord	<p>Multiple discrete (focal) lesions</p> <ul style="list-style-type: none"> - Shape: sagittal: cigar-like; axial: wedge-shaped - Size: small; ≤ 2 vertebral segments; $<$ half of the cord - Location: cervical $>$ thoracic; peripheral region; lateral and posterior columns, but central gray matter not spared - Signal characteristics: T1-hypointensity ($>$ at higher field strengths)



Gadolinium-enhancing lesions	<ul style="list-style-type: none"> - Shape: nodular; open-ring; closed-ring - Location: brain $>$ spinal cord
-------------------------------------	---

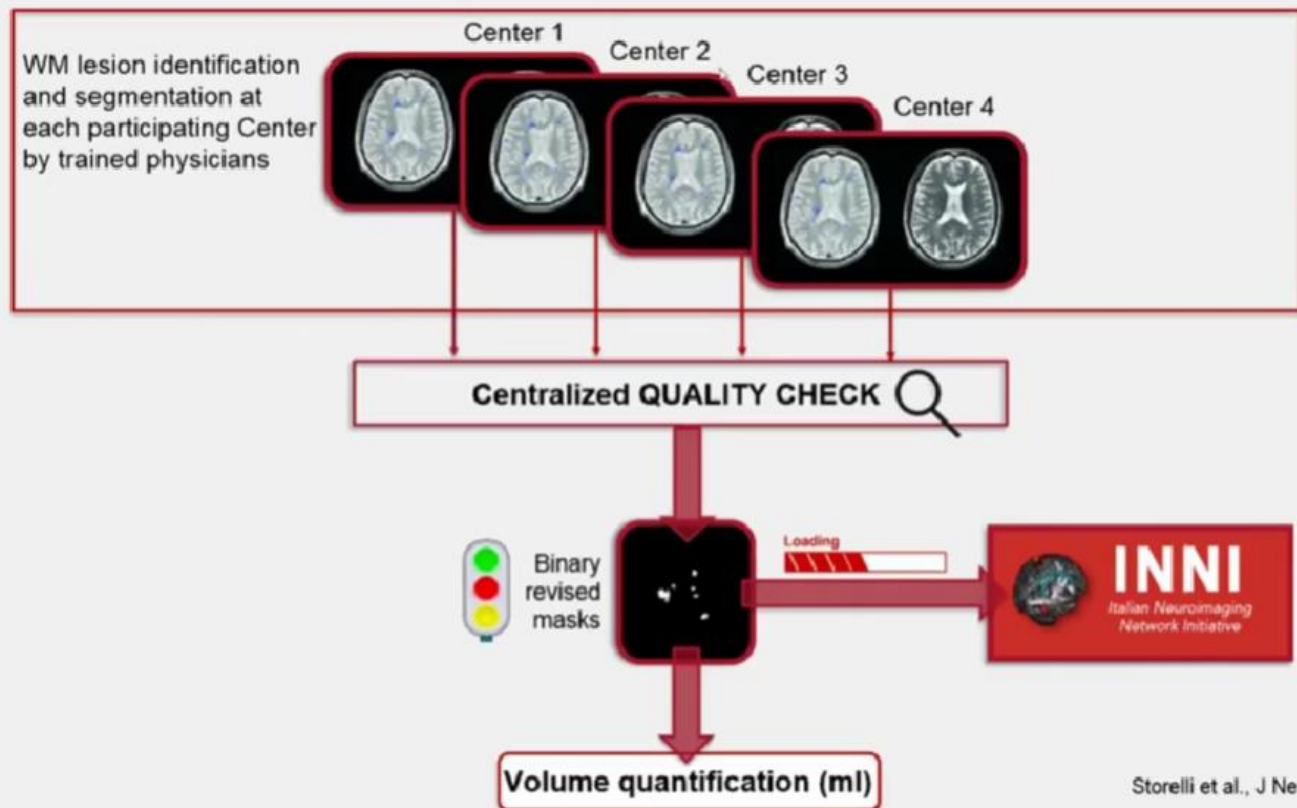


Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



INNI – Sclerosi Multipla

The INNI initiative / Lesion assessment



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



Outline

- The INNI initiative / MRI protocol
- The INNI initiative / Lesion assessment
- **The INNI initiative / Quality control**
- New automatic approaches for lesion identification and quantification
- Conclusions



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



The INNI initiative / Quality control

The collection of multicenter MRI data raises the important issues of **standardization** and **quality control**

Journal of Neurology (2019) 266:2848–2858
<https://doi.org/10.1007/s00415-019-09509-4>

ORIGINAL COMMUNICATION



MRI quality control for the Italian Neuroimaging Network Initiative: moving towards big data in multiple sclerosis

Loredana Storelli^{1,2} · Maria A. Rocca^{1,3} · Patrizia Pantano^{4,5} · Elisabetta Pagani¹ · Nicola De Stefano⁶ ·
Giacchino Tedeschi⁷ · Paola Zarin⁸ · Massimo Filippi^{1,2,3} · For the INNI Network



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



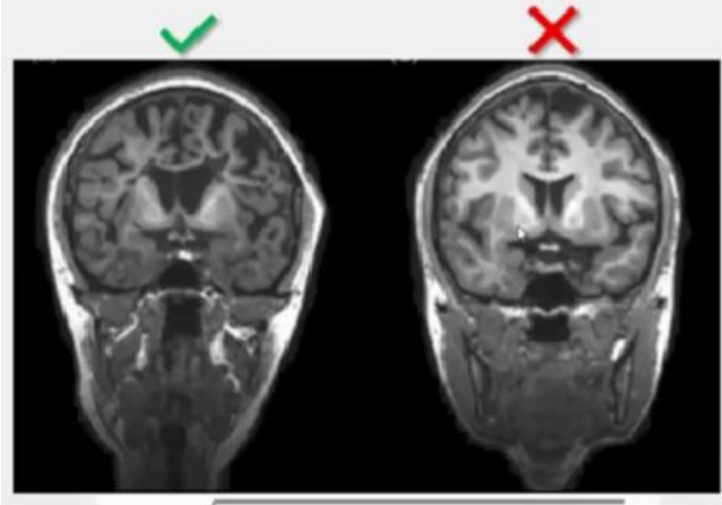
INNI – Sclerosi Multipla

The INNI initiative / Quality control

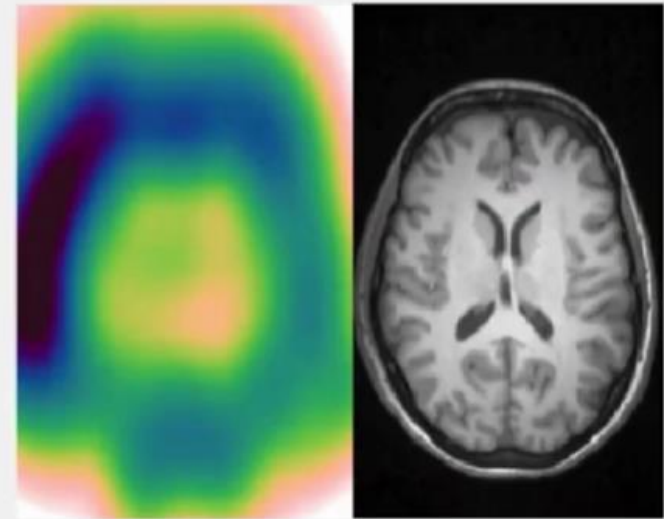
A quality control (QC) procedure is implemented to characterize and monitor the INNI database, including:

(1) Subject positioning into the MR scanner

(2) Intensity inhomogeneity



$$ED = \sqrt{(x_I - x_C)^2 + (y_I - y_C)^2 + (z_I - z_C)^2}$$



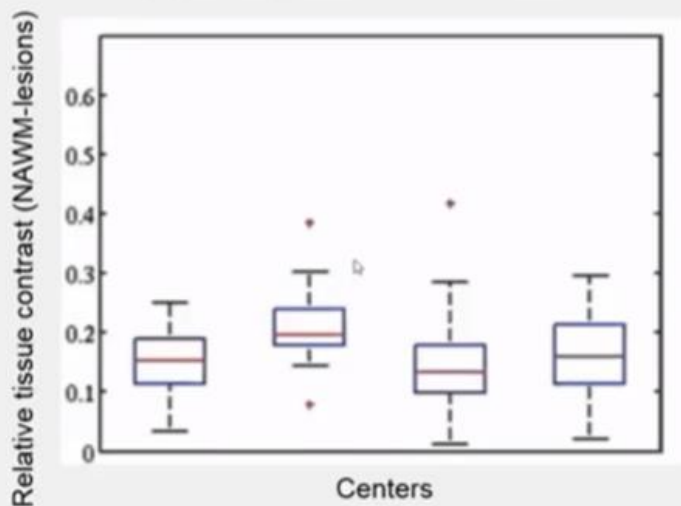
Storelli et al., J Neurol 2019



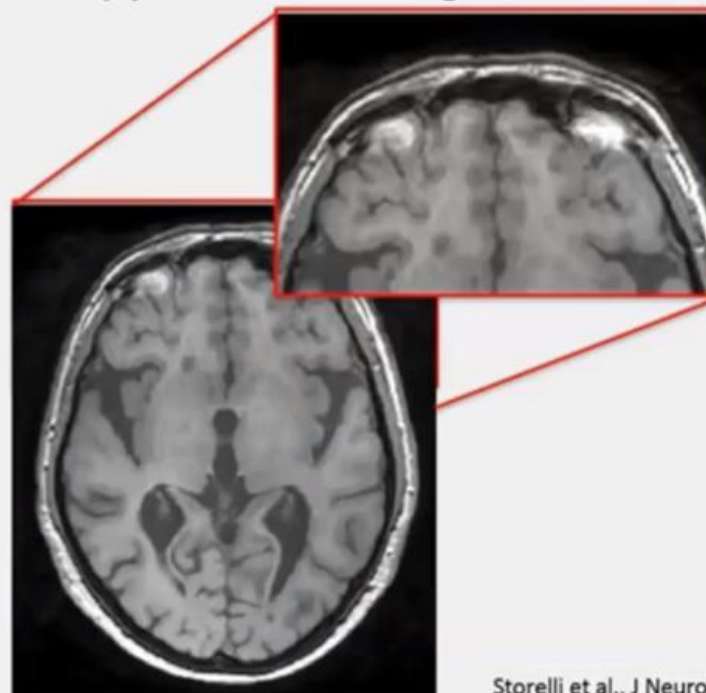
INNI – Sclerosi Multipla

The INNI initiative / Quality control

(3) Image tissue contrast



(4) Presence of image artifacts



Storelli et al., J Neurol 2019

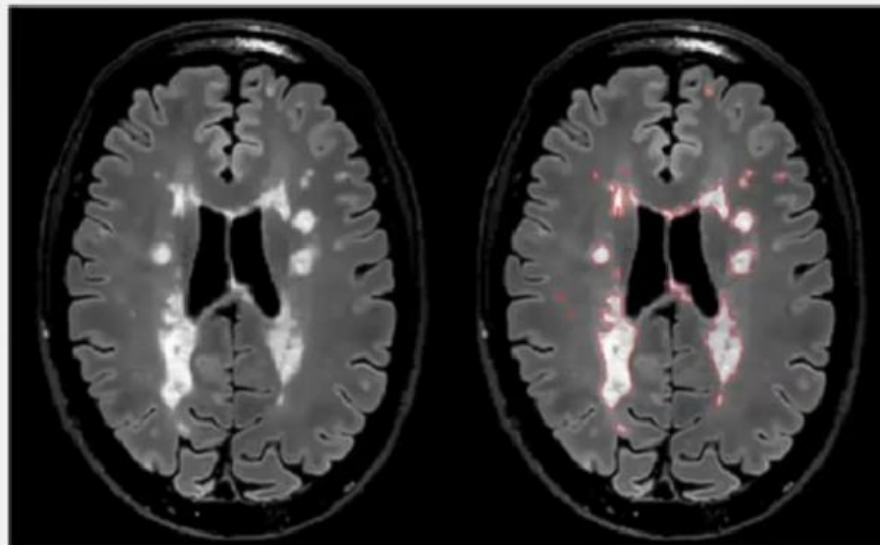


Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



The INNI initiative / Quality control

(4) Quality check and standardization of lesion assessment



1. The **best contrast** between WM, GM, and lesions is set
2. Region of interests (ROIs) should be defined using a **conservative approach** (mildly hyperintense areas around visible lesions should not be included)
3. Check on **longitudinal consistency** of lesion maps

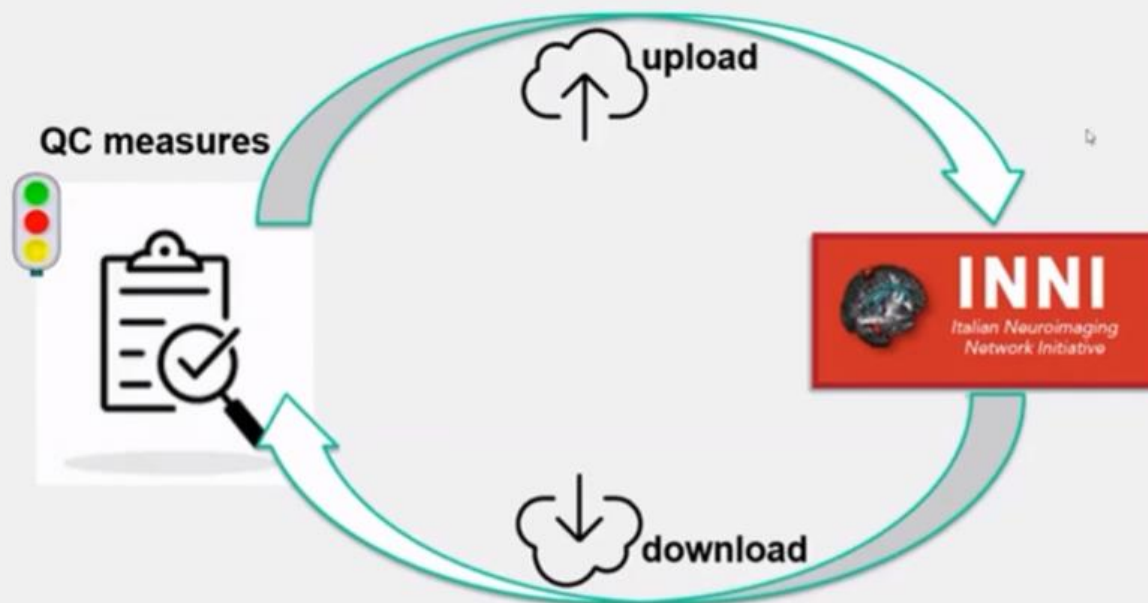


Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



INNI – Sclerosi Multipla

The INNI initiative / Quality control



- To reduce variability, the procedure of **QC and pre-processing is centralized**
- QC measures would be available together with MRI data to promote the use of a quality-assessed and standardized database



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



INNI – Sclerosi Multipla

The INNI initiative / Quality control

Patient

[Edit](#) [Delete](#)

Hash: 305495c9-148ba2cdef7547553d1299a

Site: San Raffaele Scientific Institute, Via-Salute San Raffaele University

Country: ITALY (IT)

Race: Caucasian

Fiscal code: 00aa2633d14aac098d054a597857e017

Marital state

Employment

Handedness: R

EHI: 100

Added fields and sections

Clinical

Type of onset: Monofocal

Symptoms: ON

Disease onset date (dd/mm/yyyy): 01/01/2002

Date of conversion to CDMS (dd/mm/yyyy)

Date of evolution to SPMS (dd/mm/yyyy)

Date of evolution to BMS (dd/mm/yyyy)

Date of reaching EDSS=4 (dd/mm/yyyy)

Date of reaching EDSS=6 (dd/mm/yyyy)

Neurological visit

[Patient page](#) [Edit](#) [Delete](#) [Not verified](#)

Datasets verification by the Data Controller

Actions: Site Data Manager

[New patient](#) [Search patient](#) [Import visits from CSV](#) [Update subjects from CSV](#)

Automatization of data upload

Study series

[Download CSV file](#)

Viewer	Type	Series type	Series description	Note	Quality	Primary artifact	Secondary artifact	Series ID	Number of images	Series number	Delete	Preprocessing files uploaded	Preprocessing files downloaded
View	View	Flowing State	RESTING		View			0186436-673755c-8f710084-3636263a-853643d1	3001	301	Delete	Upload	

MRI exam interface



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



un mondo libero dalla SM



Outline

- The INNI initiative / MRI protocol
- The INNI initiative / Lesion assessment
- The INNI initiative / Quality control
- **New automatic approaches for lesion identification and quantification**
- Conclusions



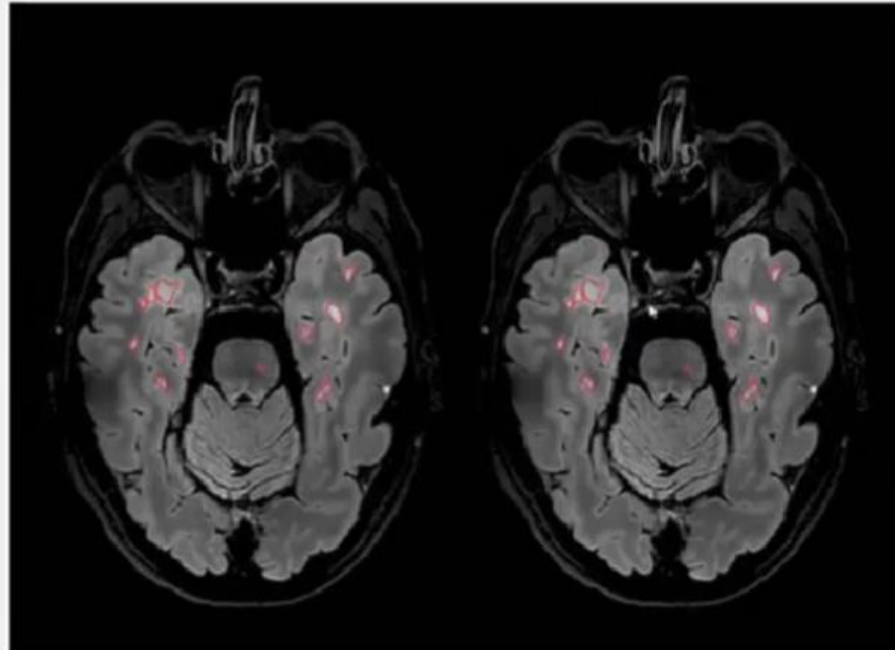
Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

**SCLE
ROSI
MULTI
PLA**
fondazione
italiana
un mondo
libero dalla SM



T2-lesion identification in MS: standard approach

- **Time-consuming**
 - 3D > 2D sequences
 - High > low lesion load
- **High intra- and inter-rater variability**



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

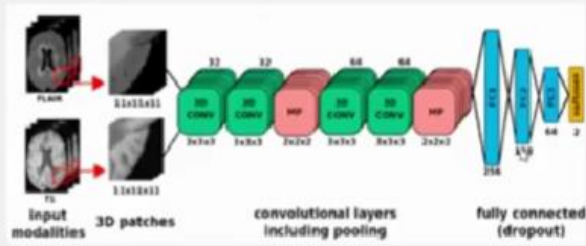
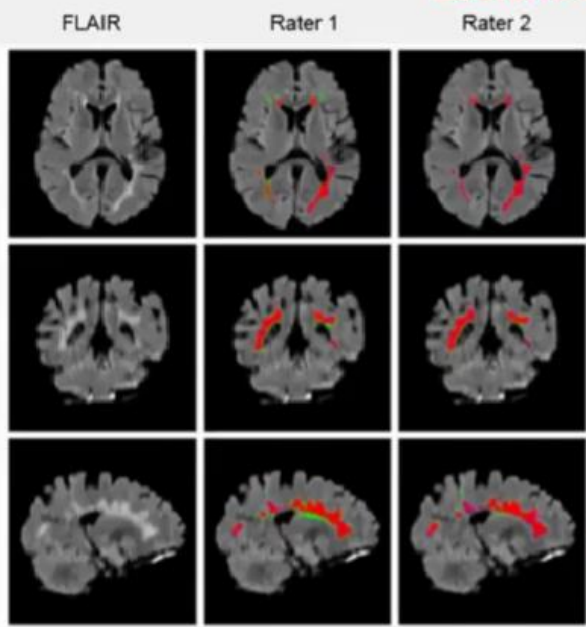


INNI – Sclerosi Multipla

T2-lesion identification in MS: new approaches

Lesions segmentation Deep learning

Astani, Dayan, Storelli et al., Neuroimage 2019



Method	DSC	Sensitivity	Precision	Score
Andermatt et al. (2017)	0.63 (0.14)	0.54 (0.19)	0.84 (0.10)	92.07
Hashemi et al. (2018)	0.66 (0.11)	0.67 (0.20)	0.71 (0.16)	91.52
Valverde et al. (2017)	0.64 (0.12)	0.57 (0.17)	0.79 (0.15)	91.44
Birnbaum and Grossman (2017)	0.63 (0.14)	0.55 (0.18)	0.80 (0.15)	91.26
Rey et al. (2014) ^a	0.52 (-)	- (-)	0.86 (-)	90.48
Deshpande et al. (2015)	0.60 (0.13)	0.55 (0.17)	0.73 (0.18)	89.81
Jain et al. (2015)	0.55 (0.14)	0.47 (0.15)	0.73 (0.20)	88.74
Shioe et al. (2010)	0.55 (0.19)	0.54 (0.15)	0.70 (0.29)	88.46
Valcarlos et al. (2018)	0.57 (0.13)	0.57 (0.18)	0.61 (0.16)	87.71
Stadler et al. (2015)	0.52 (0.14)	0.46 (0.15)	0.66 (0.18)	86.44
Full train	0.63 (0.13)	0.55 (0.16)	0.79 (0.14)	91.33
One-shot (3 layers, 26.8 ml.)	0.58 (0.16)	0.48 (0.19)	0.84 (0.13)	90.32

Valverde et al., Neuroimage 2018

Method	DSC	PPV	LTPR	LFPF	VD	SD	HD
TOADS (Shor et al., 2010)	0.5241	0.5965	0.4608	0.6277	0.4059	5.4792	13.60
LST (Schmidt et al., 2012)	0.3022	0.5193	0.1460	0.3844	0.6966	7.0919	14.35
OASIS (Dawson et al., 2013)	0.4193	0.3483	0.3755	0.4143	2.0588	3.5888	18.33
11MSY (Grossman et al., 2015)	0.6316	0.7268	0.3091	0.7307	0.3486	3.9373	9.235
OUBS	0.6655	0.8032	0.4465	0.6842	0.3372	2.5751	6.728

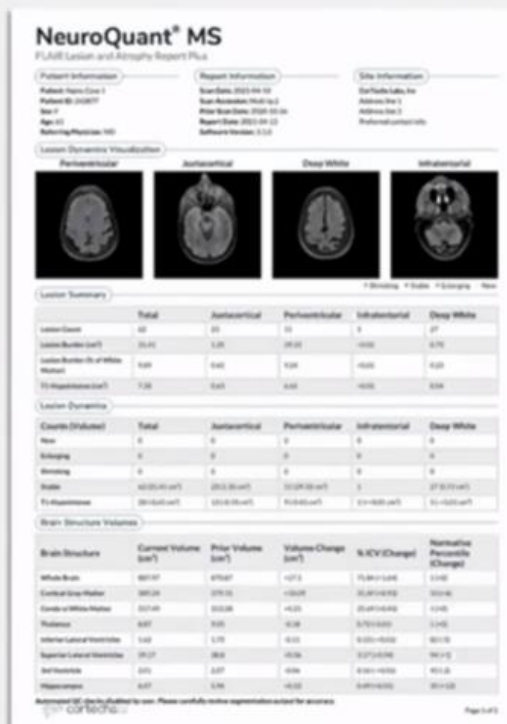
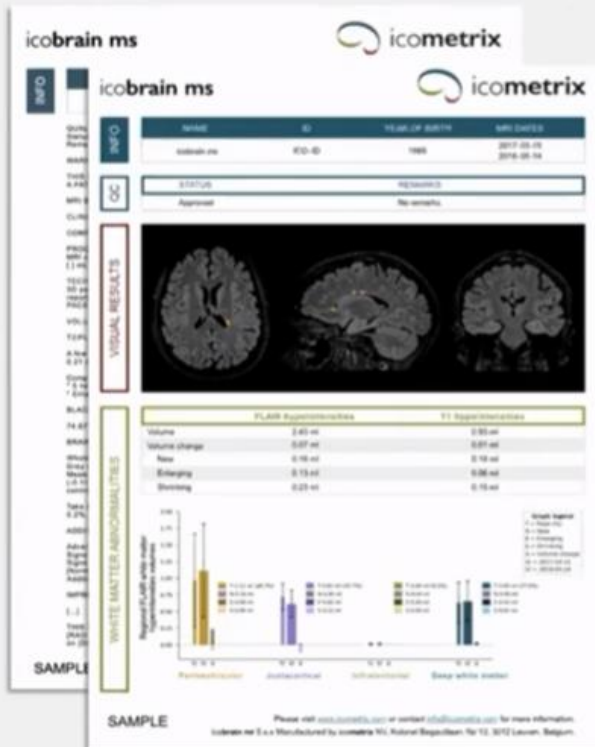


Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



INNI – Sclerosi Multipla

Automatic assessment of lesion dissemination in space and time



- Automatic reports to visualize and obtain volumetric quantification and segmentation of brain structures and lesions
- T2-hyperintense lesion distribution according to the McDonald criteria
- Directly installed on PACS



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM



un mondo libero dalla SM



Conclusions

- The creation of a standardized protocol of MRI acquisition to be applied for the study of patients with MS will provide an important step towards a better harmonization of MRI application in the MS field at a national level
- The proposed guidelines for lesion assessment are essential to apply more standardized lesion assessment criteria in MS
- Image QC is another important aspect to ensure a good quality repository for future quantitative analyses using INNI dataset
- The INNI initiative paved the way for a future standardization of MRI analysis in patients with MS
- The use of automatic approaches is appealing, but needs further validations and confirmation on larger multicenter datasets



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

**SCLE
ROSI
MULTI
PLA**
fondazione
italiana

un mondo
libero dalla SM



Ongoing effort and future steps

- Developments of methods for longitudinal assessment of T2 lesion volume and new/enlarged T2 lesions
- Inclusion of T1-hypointense lesions
- Inclusion of cortical lesions
- Verification of availability of other sequences for testing other possible MRI biomarkers (e.g., SWI, quantitative sequences)



Verso una standardizzazione per l'identificazione e misurazione delle lesioni della sostanza bianca nel paziente con SM

**SCLE
ROSI
MULTI
PLA**
fondazione
italiana

un mondo
libero dalla SM

Towards the Standardization of Brain Atrophy in MS

Nicola De Stefano

Department of Medicine, Surgery and Neuroscience
University of Siena, Italy

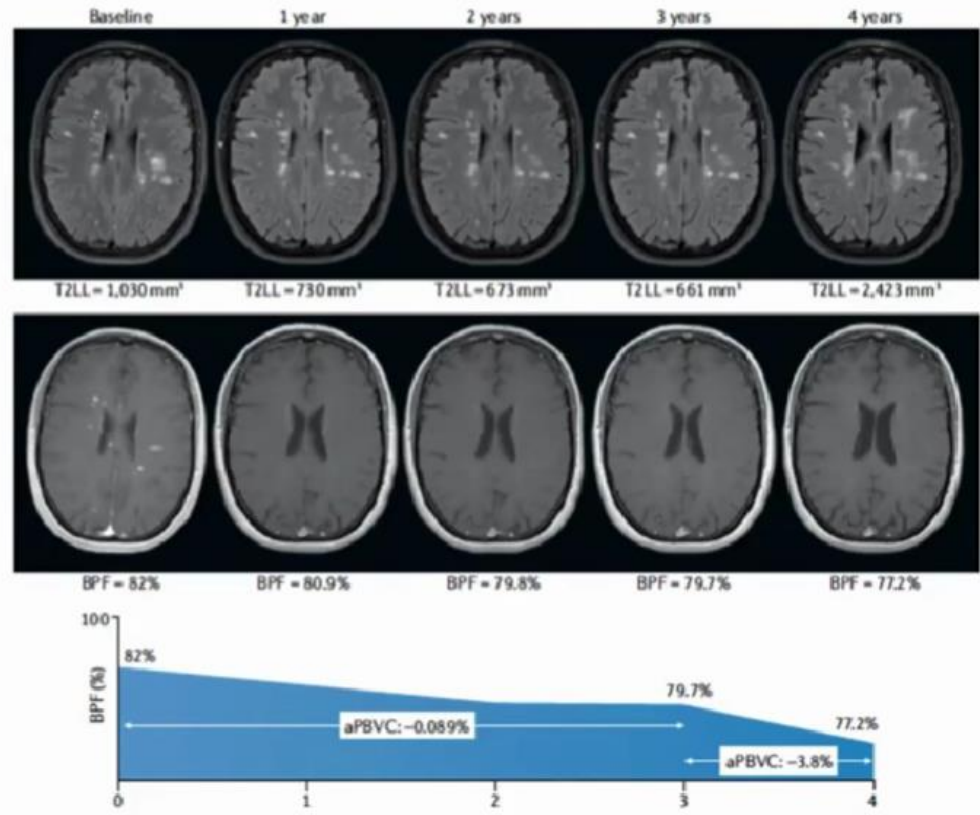


INNI – Sclerosi Multipla

MAGNIMS consensus recommendations on the use of brain and spinal cord atrophy measures in clinical practice

NATURE REVIEWS | NEUROLOGY
VOLUME 18 | MARCH 2022 | 1875

Jaume Sastre-Garriga^{1,2,3}, Deborah Pareto⁴, Marco Battaglia⁵, Maria A. Rocca⁶, Olga Ciccarelli⁶, Christian Enzinger⁷, Jens Wuerfel⁸, Maria P. Sormani^{9,10}, Frederik Barkhof^{11,12}, Tarek A. Yousry¹³, Nicola De Stefano⁴, Mar Tintore¹⁴, Massimo Filippi^{15,16}, Claudio Gasperini¹⁷, Ludwig Kappos¹⁸, Jordi Rio¹⁹, Jette Frederiksen²⁰, Jackie Palace²¹, Hugo Vrenken²², Xavier Montalban^{1,18}, Alex Rovira²³ and on behalf of the MAGNIMS study group



2

N. De Stefano

INNI – Sclerosi Multipla

JOURNAL OF MAGNETIC RESONANCE IMAGING 37:1-14 (2018)

Review

Clinical Use of Brain Volumetry

CME

Antonio Giorgio, MD, PhD and Nicola De Stefano, MD, PhD*



Use of MRI-based brain volumetry in different clinical scenarios

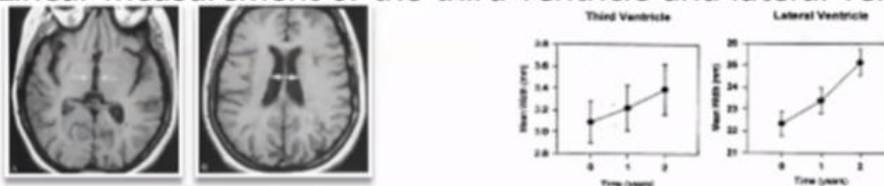
Supporting disease diagnosis	Understanding mechanisms and tracking clinical progression of disease	Monitoring treatment effect
Alzheimer's disease	Alzheimer's disease	Alzheimer's disease
Frontotemporal dementia	Multiple sclerosis	Multiple sclerosis
Focal epilepsy	Focal epilepsy	
Parkinsonisms	Headache/migraine	
	Amyotrophic lateral sclerosis	
	CADASIL	

N. De Stefano

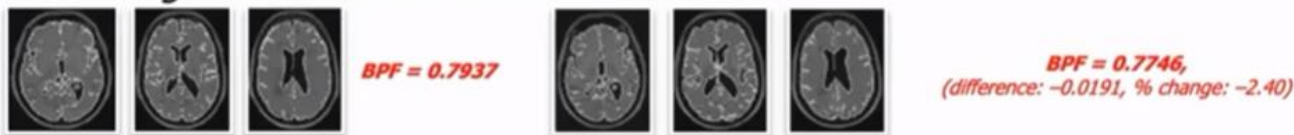
INNI – Sclerosi Multipla

MRI-Based measures to assess brain volumes

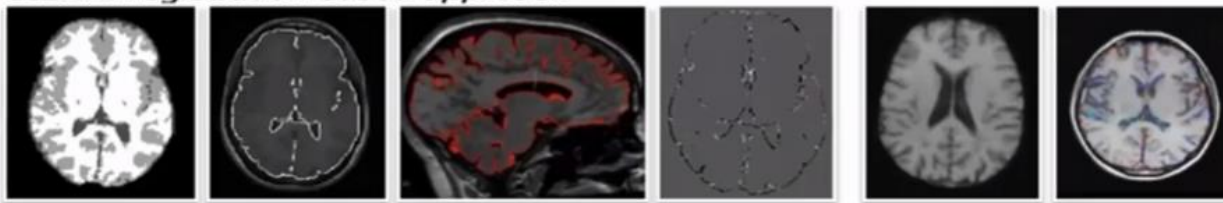
- *Linear measurement of the third ventricle and lateral ventricles²*



- *BPF: distinguishes skull and CSF from brain tissue³*



- *SIENA: registration based approach*



1. Cohen RM, et al. *Neurobiol Aging* 2006;27(10):1385-94; 2. Simon JH, et al. *Neurology* 1999;53(1):139-48; 3. Fisher E, et al. *Neurology* 2002;59(9):1412-20; 4. Battaglini M, et al. *J Neurol Sci* 2009;282(1-2):55-60

4

N. De Stefano

Challenges to the Use of BV in Clinical Practice

Category	Topic
Physiological factors [11, 57, 64, 66, 70, 74, 75]	Age
	Body mass index
	Diurnal variation
	Genotype (ApoE expression)
	Hydration state
	Menstrual cycle
Disease-related factors [11, 57, 64, 74–77]	Fluid-level changes attributable to inflammation (edema)
	Fluid-level changes attributable to resolution of inflammation (treatment-related pseudoatrophy)
Habits and comorbidities [11, 64, 66, 74]	Alcohol consumption
	Cardiovascular hypertension
	Diabetes mellitus
	Obesity
	Smoking
	MRI-related factors [11, 57, 64, 65, 74, 76]
Changes in scanner type and scanner upgrades	
Factors influencing scan quality (head motion, distortions, inhomogeneity artifacts)	
Measurement error	
Non-standardized quantification methods	
Patient repositioning in the scanner	
Reimbursement	
Complexity of use (e.g. PACS integration)	
Logistical factors [11, 57, 64, 65, 76]	Lack of normative data
	Methods dependent on real-time data
	Poor integration of some image formats

Challenges to the Use of BV in Clinical Practice

- ❖ MRI Acquisition
- ❖ MRI Analysis
- ❖ Data interpretation

De Stefano et al CNS Drugs 2017

6

N. De Stefano

INNI – Sclerosi Multipla

MRI Acquisition for Volumetry - GE

GE 1.5T Signa Excite, Discovery, Optima, Brivo, Voyager, Creator, Explorer & Artist Excite, Discovery, Pioneer, Architect and Premier		GE 3T Signa			
Sequence name		1.5 T C-Spine 3D IR-FSPGR	1.5 T Brain 3D IR-FSPGR	3 T C-Spine 3D IR-FSPGR	3 T Brain 3D IR-FSPGR
Imaging parameters	Plane	Sagittal	Sagittal	Sagittal	Sagittal
	Mode	3D	3D	3D	3D
	Pulse sequence	FSPGR	FSPGR	FSPGR	FSPGR
	Grad Mode (twinspeed only)	Zoom	Zoom	Zoom	Zoom
	Imaging options	EDR, Fast, IR prep, Asset/ARC	EDR, Fast, IR prep, Asset/ARC	EDR, Fast, IR prep, Asset/ARC	EDR, Fast, IR prep, Asset/ARC
Acquisition	Freq. FOV	25.0	25.0	25.0	25.0
	Phase FOV	1.0	1.0	1.0	1.0
	Slice thickness	1.0	1.0	1.0	1.0
	Spacing (2D)				
	Freq Dir	SI	SI	SI	SI
	TR (ms)	-	-	-	-
	# slices / locs per slab	192	192	192	192
	Chem SAT				
Details	# of TE(s) per scan	1	1	1	1
	Num shots				
	TE (ms)	Min Full	Min Full	Min Full	Min Full
	Flip angle	12	12	11	11
	Prep Time/T1 (ms)	400	400	450	450
	ETL				
	Intensity Correction	PURE	PURE	PURE	PURE
	Intensity Filter	None	None	None	None
	3D Geometry Corr	Yes	Yes	Yes	Yes
	Frequency	256	256	256	256
	Phase	256	256	256	256
	NEX	1	1	1	1
	Bandwidth (kHz)	22.5	22.5	22.73	22.73
	Flow comp direction	-	-	-	-
Acceleration	Phase	1,75/2	1,75/2	1,75/2	1,75/2
	Slice	1/1,5	1/1,5	1/1,5	1/1,5
Additional instructions	User CV	Excitation = Slab Selective	Excitation = NON Selective	Excitation = Slab Selective	Excitation = NON Selective
	Other	No ZIP2. No ZIP512. Use of HyperSense is allowed if available.	No ZIP2. No ZIP512. Use of HyperSense is allowed if available.	No ZIP2. No ZIP512. Use of HyperSense is allowed if available.	No ZIP2. No ZIP512. Use of HyperSense is allowed if available.
Scan info	Imaging time	-4:40	-4:40	-4:40	-4:40

7

INNI – Sclerosi Multipla

MRI Acquisition for Volumetry - Siemens

		Siemens 1.5T SymphonyTim, Espree, Essenza, Avanto, Amira, Aera, Sempra and Sola Verio, Skyra, Spectra, Prisma, Biograph mMR, Vida and Lumina		Siemens 3T Trio,	
		1.5 T	1.5 T	3 T	3 T
		Spine 3D MP-RAGE	Brain 3D MP-RAGE	Spine 3D MP-RAGE	Brain 3D MP-RAGE
Sequence name	Sequence variant	*tfl3d1_ms	*tfl3d1_ms	*tfl3d1_ms	*tfl3d1_ms
Routine	Orientation	Sagittal	Sagittal	Sagittal	Sagittal
	Phase enc. direction	A >> P	A >> P	A >> P	A >> P
	Phase oversampling [%]	0 - 16,7	0 - 16,7	0 - 16,7	0 - 16,7
	Slice oversampling [%]	12.5	16.7	12.5	16.7
	Slices per group/slab	192	192	192	192
	FOV read [mm]	250	250	250	250
	FOV phase [%]	100	100	100	100
	Slice thickness [mm]	1.0	1.0	1.0	1.0
	Distance factor [%]				
	TR [ms]	2200/2300	2200/2300	2300/2400	2300/2400
	TE [ms]	minimum	minimum	minimum	minimum
	Averages	1	1	1	1
	Concatenations				
	Contrast	Measurements	1	1	1
Magn. preparation		Sel IR	Non-Sel IR	Sel IR	Non-Sel IR
TI [ms]		900/950	900/950	900/1050	900/1050
Flip Angle		8	8	9	9
Fat suppr.		None	None	None	None
Resolution	Base resolution	256	256	256	256
	Phase resolution [%]	100	100	100	100
	Slice resolution [%]	100	100	100	100
	Phase partial Fourier	Off	Off	Off	Off
	Slice partial Fourier	Off	Off	Off	Off
	Filter	Prescan Normalize, Elliptical Filter Distortion Corr. 3D	Prescan Normalize, Elliptical Filter Distortion Corr. 3D	Prescan Normalize, Elliptical Filter Distortion Corr. 3D	Prescan Normalize, Elliptical Filter Distortion Corr. 3D
	Interpolation	Off	Off	Off	Off
iPAT	Grappa/CAIPIRIHA acceleration AP = 2, Acceleration RL= 1	Grappa/CAIPIRIHA acceleration AP = 2, Acceleration RL= 1	Grappa/CAIPIRIHA acceleration AP = 2, Acceleration RL= 1 - 2	Grappa/CAIPIRIHA acceleration AP = 2, Acceleration RL= 1 - 2	
Sequence	Contrasts				
	Bandwidth [Hz/Px]	130	130	190	190
	Flow comp.	No	No	No	No
	Asymmetric echo	Allowed	Allowed	Allowed	Allowed
	Turbo factor				
	Gradient mode	Fast	Fast	Fast	Fast
	Excitation	Non-sel.	Non-sel.	Non-sel.	Non-sel.
	RF spoiling	On	On	On	On
Additional instructions	USE of GRASP is allowed if available	USE of GRASP is allowed if available	USE of GRASP is allowed if available	USE of GRASP is allowed if available	
Approximate scan time [min:sec]	-5:00	-5:00	-5:00	-5:00	

8

N. De Stefano

INNI – Sclerosi Multipla

MRI Acquisition for Volumetry - Philips

PROTOCOL FOR sagittal 3D T1-W OF THE BRAIN AND C-SPINE Philips 1.5 T & 3 T (Intera, Achieva, and Ingenia)					
		1.5 T	1.5 T	3 T	3 T
Sequence name		Spine 3D BrainVIEW T1	Brain 3D BrainVIEW T1	Spine 3D BrainVIEW T1	Brain 3D T1
Geometry	CLEAR	yes	yes	yes	yes
	FOV (mm)	250 (AP) × 250 (FH) × 192 (RL)	250 (AP) × 250 (FH) × 192 (RL)	250 (AP) × 250 (FH) × 192 (RL)	250 (AP) × 250 (FH) × 192 (RL)
	RFOV (%)	100	100	100	100
	Foldover suppression	no	no	no	no
	Voxel size (mm)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)
	Recon voxel size (mm)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)	0.98 (AP) × 0.98 (FH) × 1.0 (RL)
	Matrix scan	256	256	256	256
	Reconstruction matrix	256	256	256	256
	Scan percentage (%)	100	100	100	100
	SENSE	S reduction (RL) = 2, P reduction (AP) = 1, P as factor = 1	S reduction (RL) = 2, P reduction (AP) = 1, P as factor = 1	S reduction (RL) = 2, P reduction (AP) = 1, P as factor = 1	S reduction (RL) = 2, P reduction (AP) = 1, P as factor = 1
	Slices	192	192	192	192
	Slice thickness (mm)	1.0	1.0	1.0	1.0
	Slice gap (mm)	overcontiguous = no	overcontiguous = no	overcontiguous = no	overcontiguous = no
	Slice orientation	sagittal	sagittal	sagittal	sagittal
	Contrast	Foldover direction	AP	AP	AP
Fat shift direction		F	F	F	F
Rest slabs		0	0	0	0
Scan mode		3D	3D	3D	3D
Technique		FFE	FFE	FFE	FFE
Contrast enhancement		T1	T1	T1	T1
Fast Imaging mode		TFE	TFE	TFE	TFE
Shot mode		multishot	multishot	multishot	multishot
TFE factor		254	254	254	254
Shot Interval (ms)		shortest	shortest	shortest	shortest
Profile order		linear	linear	linear	linear
Echoes		1	1	1	1
Partial echo		no	no	no	no
TE (ms)		shortest	shortest	shortest	shortest
Flip angle (deg)		8	8	8	8
TR (ms)	shortest	shortest	shortest	shortest	
Motion	Half Scan	no	no	no	no
	Water fat shift	0,8/1,6 (user-defined)	0,8/1,6 (user-defined)	1,8/2 (user-defined)	1,8/2 (user-defined)
	Fat suppression	no	no	no	no
	TFE / IR prepulse	invert	invert	invert	invert
	Slice selection	no	no	no	no
	TI (ms)	950 (TFE prepulse delay)	950 (TFE prepulse delay)	1060 (TFE prepulse delay)	1060 (TFE prepulse delay)
	Diffusion mode	no	no	no	no
	Flow compensation	no	no	no	no
	NSA	1	1	1	1
	Other	USE of CompressedSENSE is allowed if available	USE of CompressedSENSE is allowed if available	USE of CompressedSENSE is allowed if available	USE of CompressedSENSE is allowed if available
Approximate scan time	-5:00	-5:00	-5:00	-5:00	

9

N. De Stefano

Brain MRI acquisition protocol

3DT1 Sagittal View



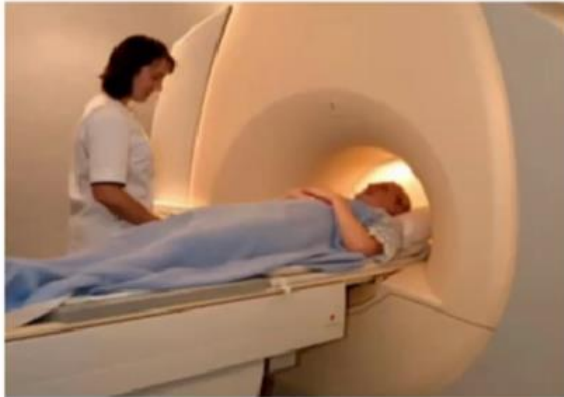
Slice Thickness: 1mm
N. Slices: variable, depending on neck length



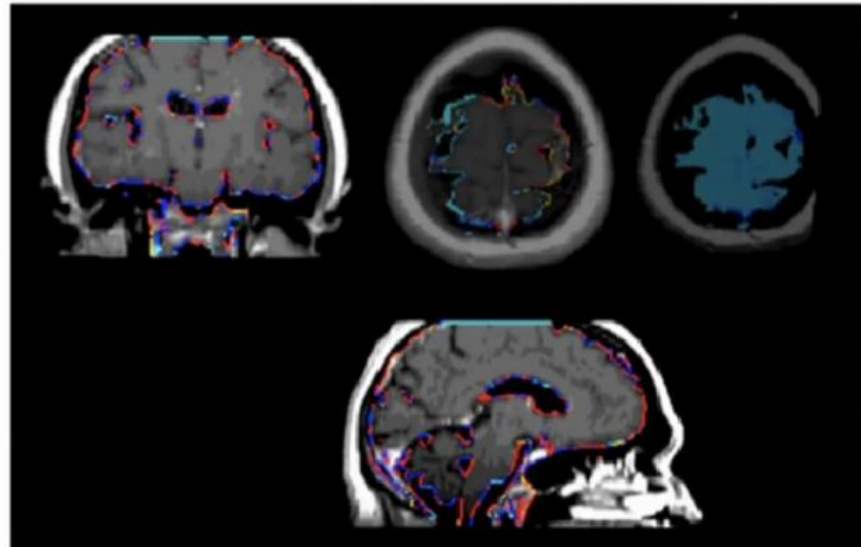
1st visible disc from the top

Image Acquisition – Data Quality

Patient/Operator



Partial head acquisition



Courtesy of Department of Medicine, Surgery and NeuroScience,
University of Siena, Italy.

11

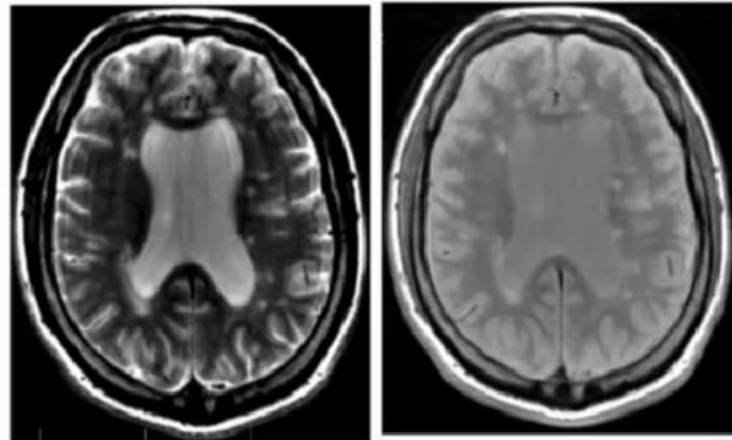
N. De Stefano

Image Acquisition – Data Quality

Patient/Operator



Intensity and movement artifacts



Courtesy of Department of Medicine, Surgery and NeuroScience,
University of Siena, Italy.

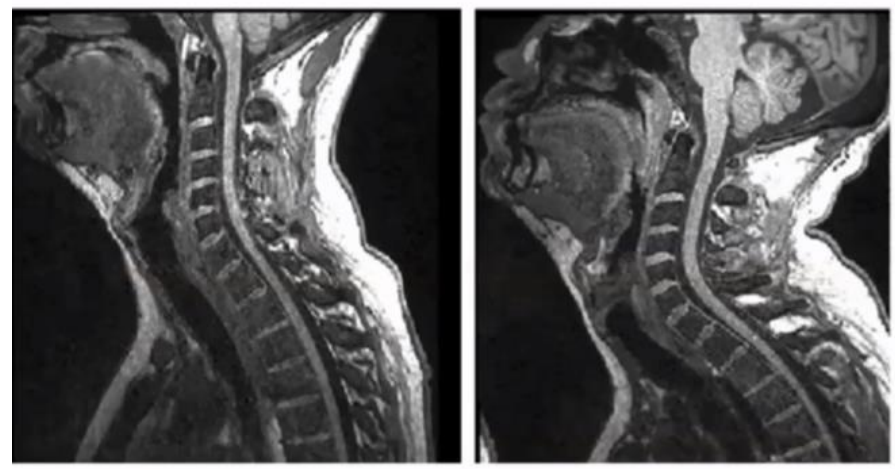
12

N. De Stefano

INNI – Sclerosi Multipla

Image Acquisition – Data Quality

- Incorrect repositioning



Baseline

Courtesy of Paola Valsalsina
& Mara Rocca

Follow-up



N. De Stefano

INNI – Sclerosi Multipla

Estimating and accounting for the effect of MRI scanner changes on longitudinal whole-brain volume change measurements

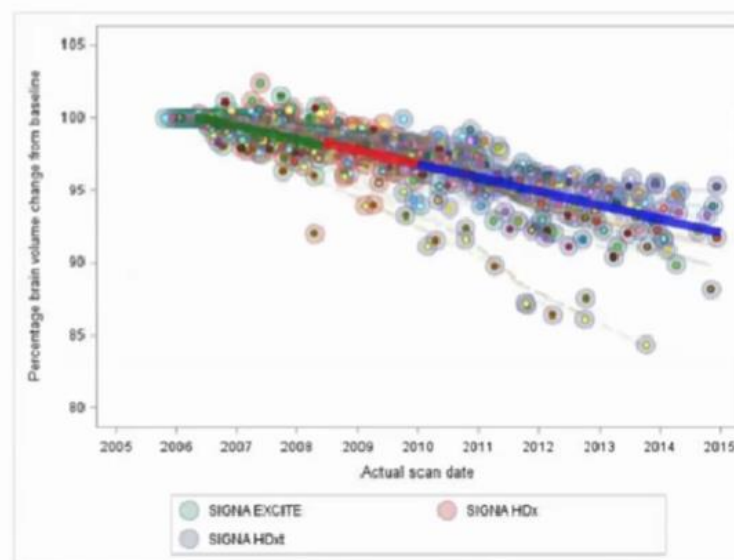
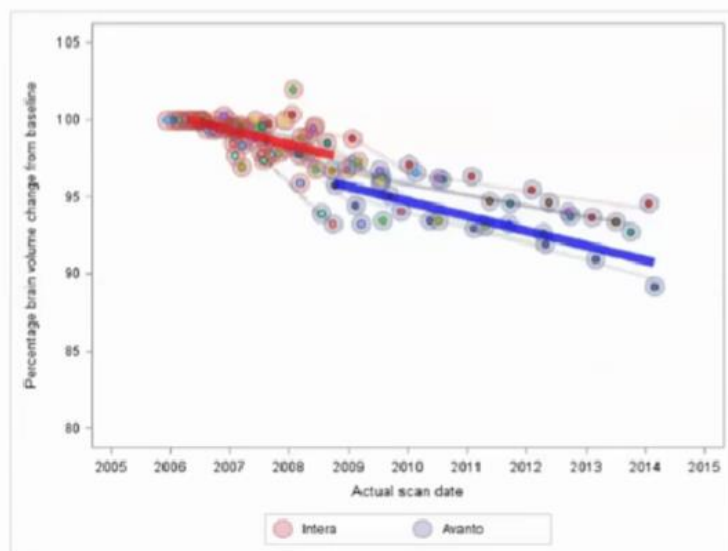


Hyunwoo Lee^{a,*}, Kunio Nakamura^b, Sridar Narayanan^a, Robert A. Brown^a, Douglas L. Arnold^a,
for the Alzheimer's Disease Neuroimaging Initiative¹

^a Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

NeuroImage 184 (2019) 555-565

^b Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA



N. De Stefano

INNI – Sclerosi Multipla

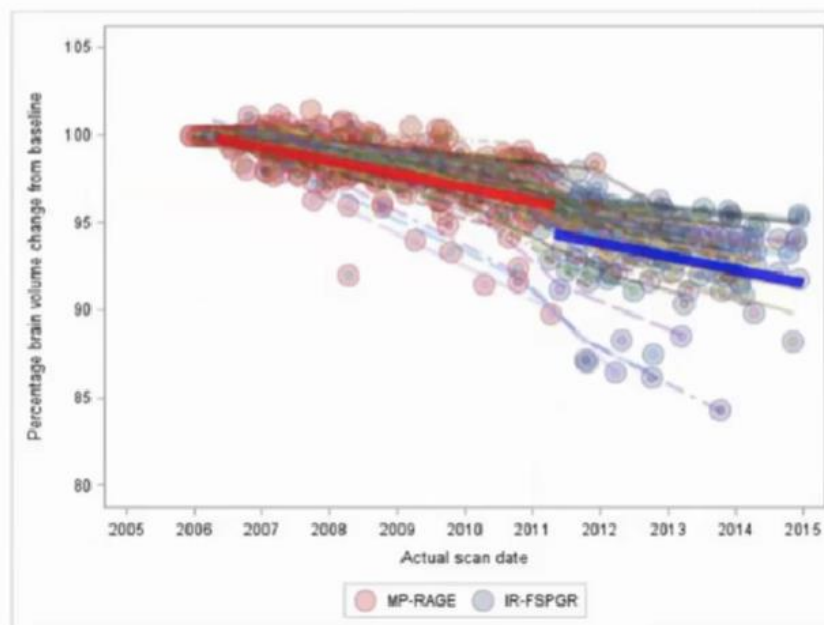
Estimating and accounting for the effect of MRI scanner changes on longitudinal whole-brain volume change measurements

Hyunwoo Lee^{a,*}, Kunio Nakamura^b, Sridar Narayanan^a, Robert A. Brown^a, Douglas L. Arnold^a,
for the Alzheimer's Disease Neuroimaging Initiative¹

^a Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

^b Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA

NeuroImage 184 (2019) 555–565

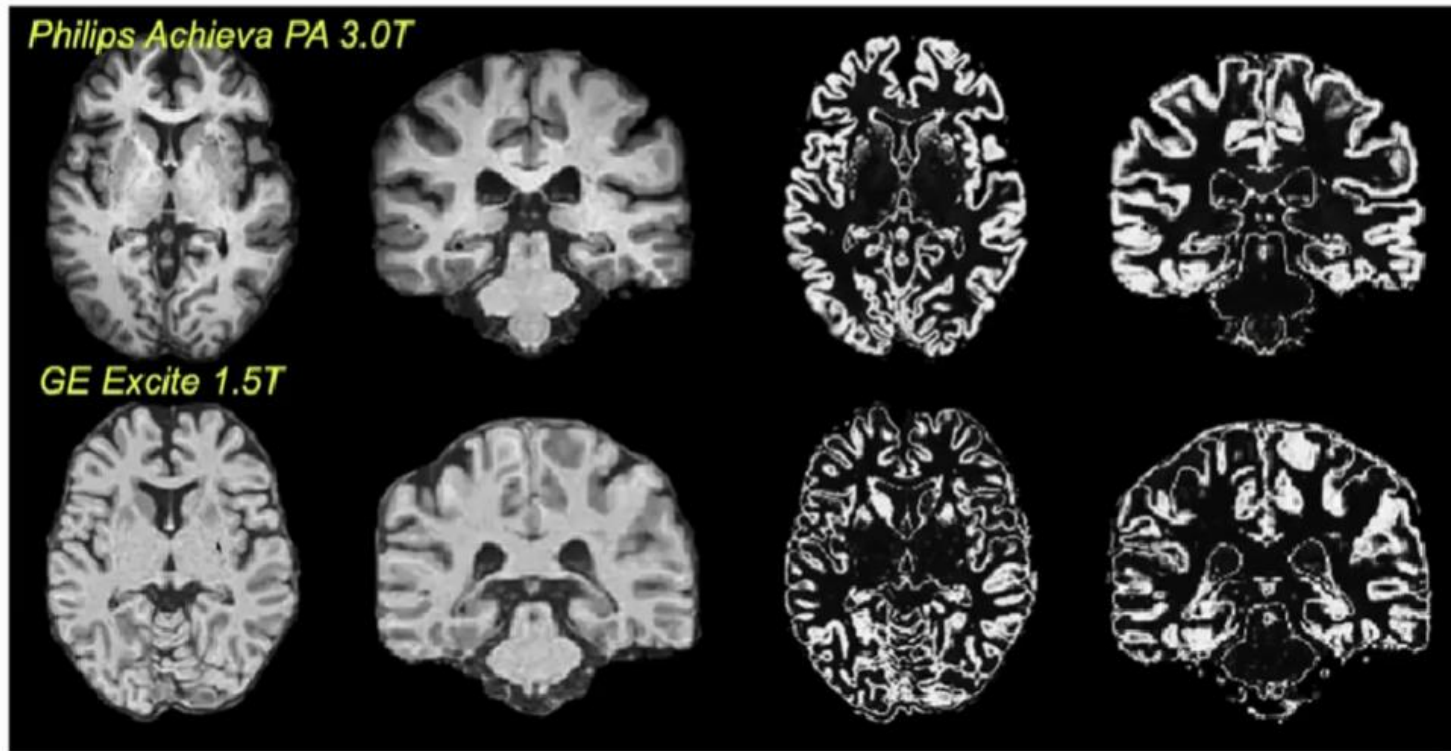


15

N. De Stefano

INNI – Sclerosi Multipla

Image Acquisition – The issue of standardization



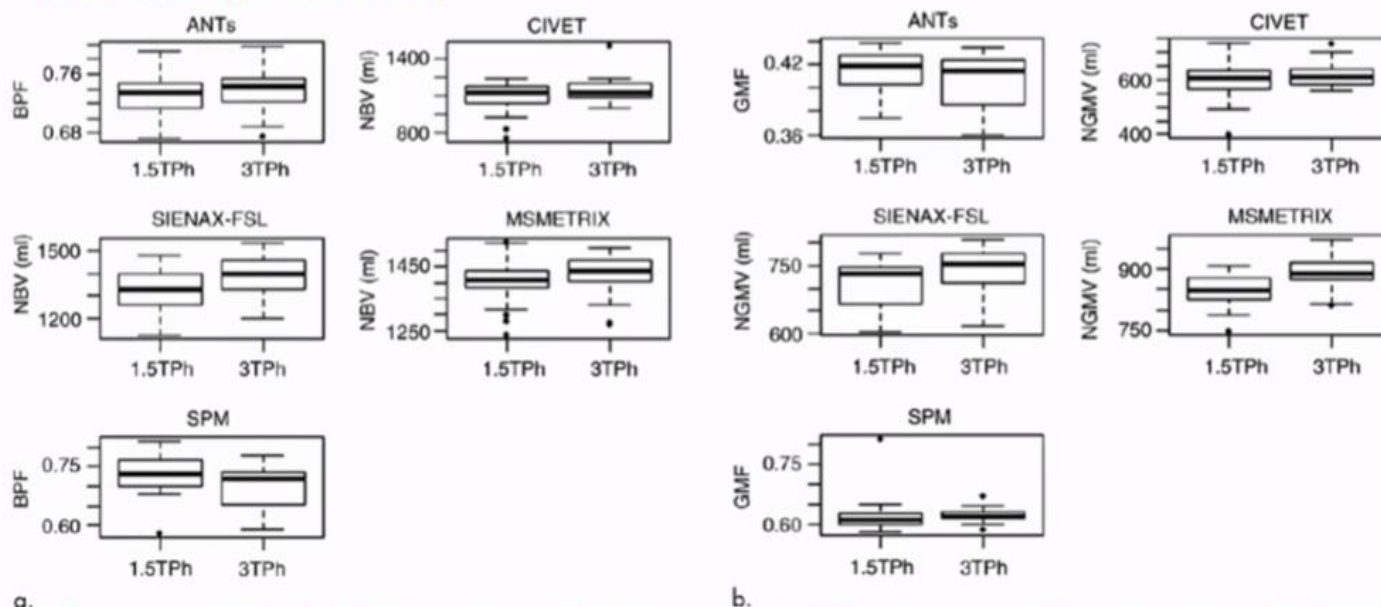
Krugel et al Neuroimage 2010

INNI – Sclerosi Multipla

Measurement of Whole-Brain and Gray Matter Atrophy in Multiple Sclerosis: Assessment with MR Imaging

Loredana Storelli, MSc • Maria A. Rocca, MD • Elisabetta Pagani, MSc • Wim Van Hecke, PhD • Mark A. Horsfield, PhD • Nicola De Stefano, MD, PhD • Alex Rovira, MD • Jaume Sastre-Garriga, MD • Jacqueline Palace, MD • Diana Sima, PhD • Dirk Smeets, PhD • Massimo Filippi, MD • for the MAGNIMS Study Group

• 19 MS (Philips 1.5T & 3T)



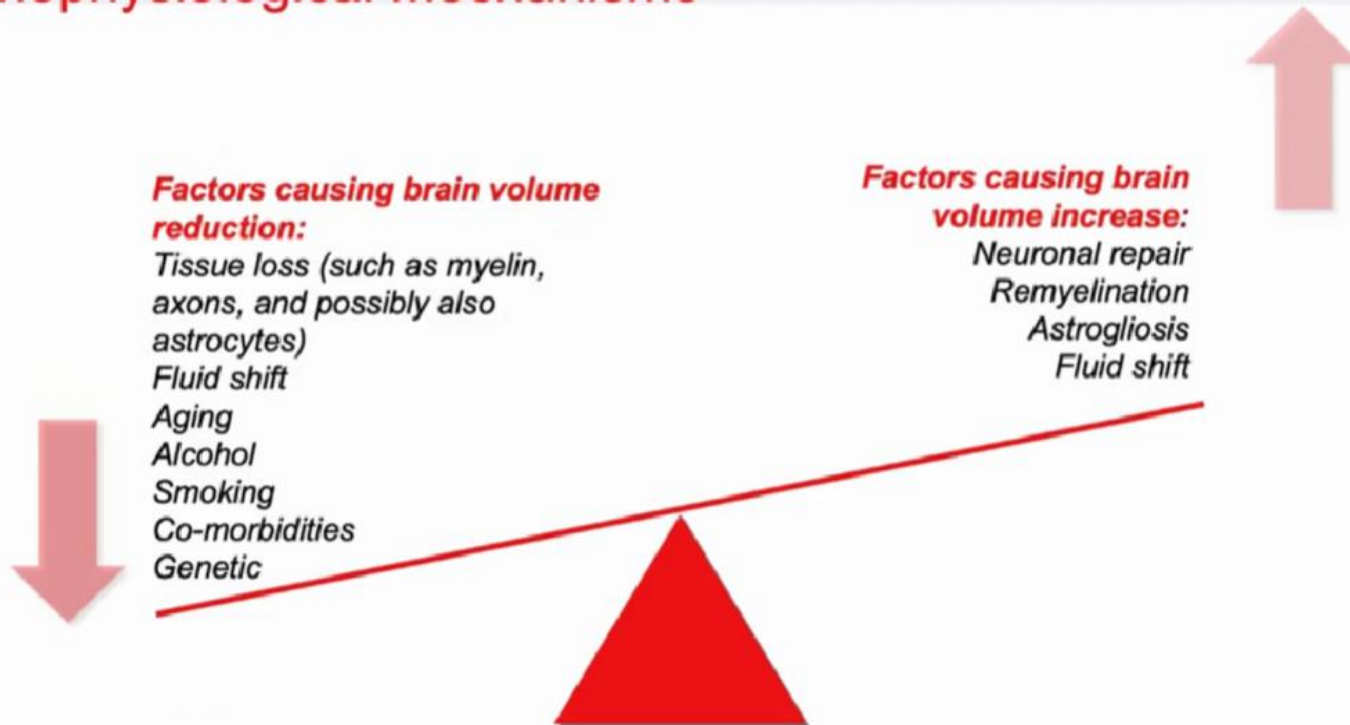
- Great repeatability (within system), but poor reproducibility (among different systems/field strengths)
- An improved reproducibility is required for clinical application

17

N. De Stefano

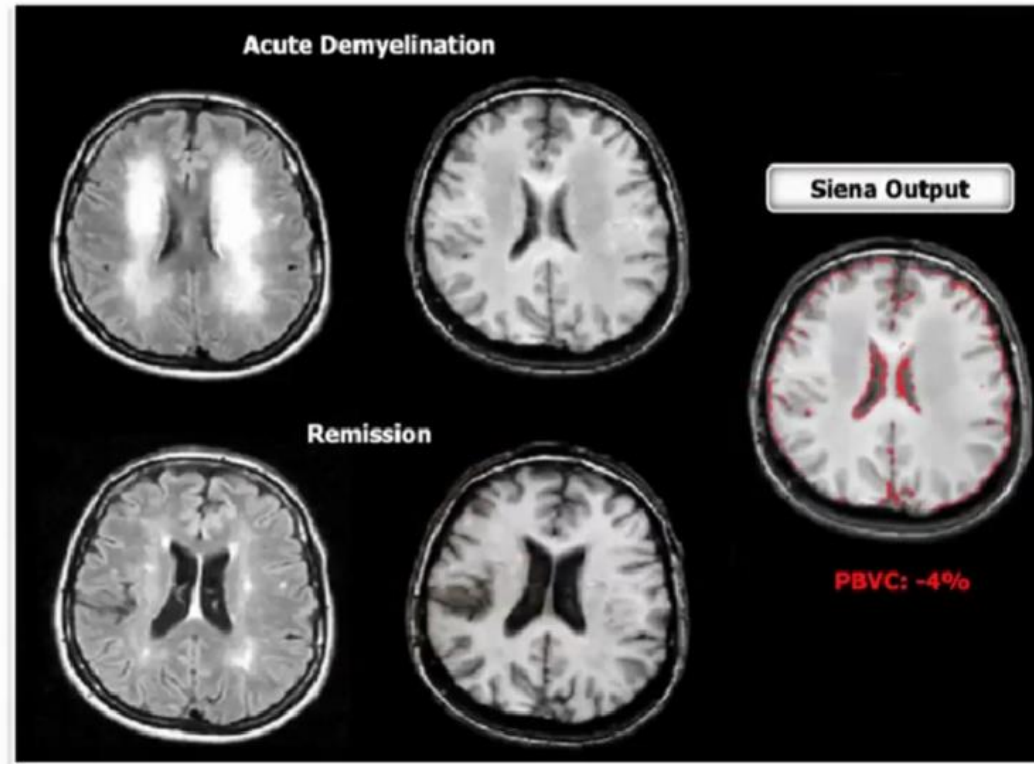
INNI – Sclerosi Multipla

Brain Volume Change: A Composite of Multiple Pathophysiological Mechanisms



N. De Stefano

Interpreting Brain Atrophy in MS Pseudoatrophy



Giorgio A, et al. J Magn Reson Imaging 2013;37(1):1-14

N. De Stefano

INNI – Sclerosi Multipla

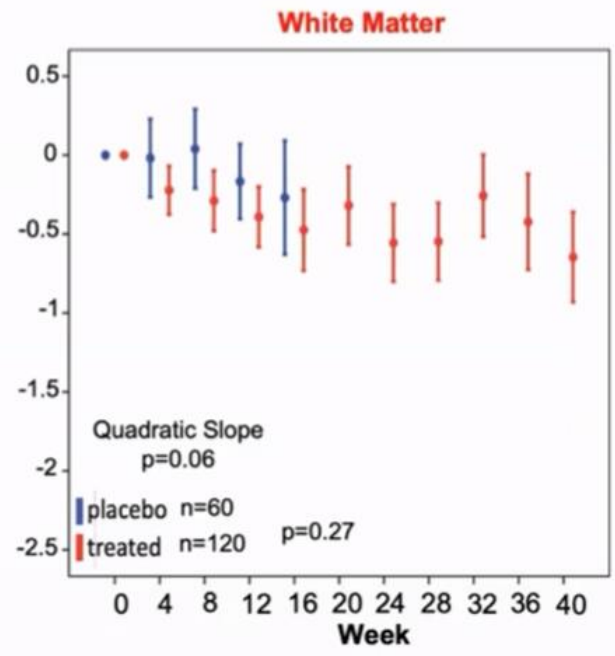
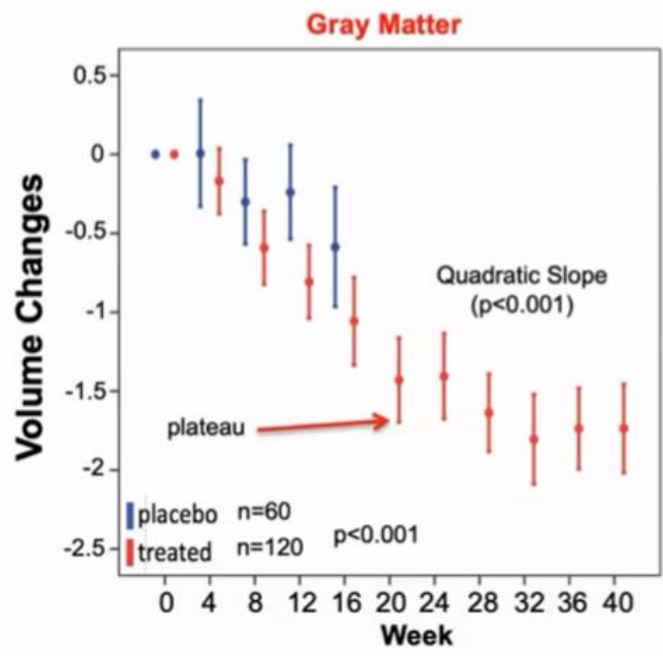


RESEARCH ARTICLE Annals of Clinical and Translational Neurology 2021; 8(2): 623-630

Dynamics of pseudo-atrophy in RRMS reveals predominant gray matter compartmentalization

Nicola De Stefano¹, Antonio Giorgio¹, Giordano Gentile¹, Maria Laura Stromillo¹, Rosa Cortese¹, Claudio Gasperini², Andrea Visconti³, Maria Pia Sormani⁴ & Marco Battaglini¹

¹Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy
²San Camillo-Forlanini Hospital, Rome, Italy
³Medical Affairs Department, Merck Serono, Rome, Italy
⁴Biostatistics Unit, Department of Health Sciences, University of Genoa, Genoa, Italy



20

N. De Stefano

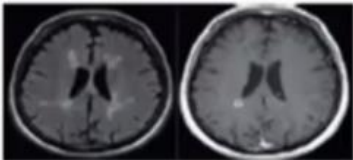
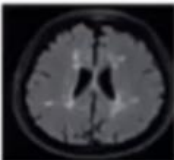
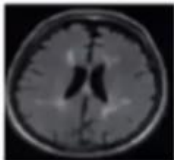
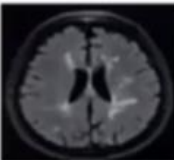
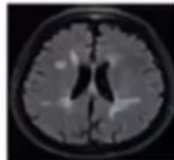


apr. '23



INNI – Sclerosi Multipla

Standardised brain MRI protocol for 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
				

Magnetic field strength: 3T (recommended, not mandatory)

Spatial resolution:

2D: 3 mm slice thickness (no gap), in-plane 1x1 mm

3D: isotropic voxel size 1x1x1 mm

Wattjes MP...Rovira A. *Lancet Neurol* 2021;20:653-670
Rovira A et al. *Nat Rev Neurol* 2015;11:471-82
Wattjes MP et al. *Nat Rev Neurol* 2015; 11: 597-606



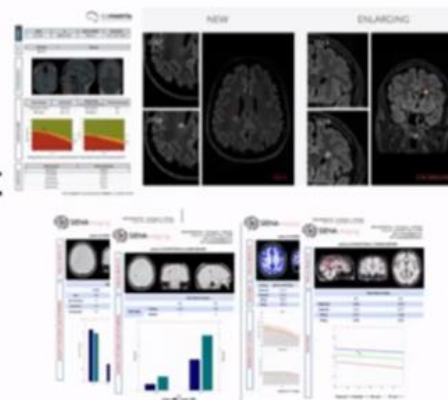
N. De Stefano

Can we assess brain atrophy in the single patient?

- ❖ Increasing desire to use measures of brain volumes in clinical setting.
 - ❖ To assess prognosis
 - ❖ To monitor treatment effect

Integrated Platforms for MRI Quantification

- ✓ BrainMagix - amagylis
- ✓ Icobrain MS – icometrix
- ✓ Lesion Quant – Neuroquant
- ✓ Quantib ND - quantib
- ✓ Olea – subtraction module
- ✓ SIENA Imaging - SinLab



un mondo libero dalla SM

N. De Stefano

Conclusions

- ◆ MRI-derived measures of brain volumes are feasible, sensitive to changes and clinically relevant. Need of **standardised MRI** acquisition
- ◆ Issues with **data processing**. To be done in specialized centres
- ◆ Issue with **data interpretation** (e.g. confounding factors). To be done by the clinician.
- ◆ Increasing desire to use measures of brain volumes in the clinical setting. **Difficult for single patient assessment.**



N. De Stefano

21 Giugno 2022 - Corso Virtuale
"The Italian neuroimaging network initiative (INNI): verso la standardizzazione dell'utilizzo della RM nel paziente con sclerosi multipla a livello nazionale"



Collaborazione con il Registro SM: condivisione della survey conoscitiva

Antonio Gallo
Centro SM – 3TMRI Research Center
Dipartimento "DAMSS"
Università della Campania "Luigi Vanvitelli"



A. Gallo

REGISTRO ITALIANO SCLEROSI MULTIPLA

Esordio

Data esordio SM
01/08/1996

Note: è obbligatorio inserire Data esordio SM oppure selezionare RIS-Si in caso di Sindrome Radiologicamente Isolata

RIS
 Si No
 Data RIS
 gg/mm/aaaa

Sintomi troncocefalici
 Si No

Sintomi vie ottiche
 Si No

Sintomi midollo spinale
 Si No

Sintomi sopratentoriali
 Si No

Altri sintomi
 Si No

Specificare

Progressione all'esordio
 Si No

Data inizio progressione
 15/06/2007

Diagnosi

Data diagnosi
 05/03/1997

Criterio conferma diagnosi → Criterio conferma diagnosi

Diagnosi SM

- Diagnosi SM
- Seleziona**
- Diagnosi SM
- NMO
- NMO Spectrum
- No SM
- Possibile SM
- SM secondo McDonald 2001
- SM secondo McDonald 2010
- SM secondo McDonald 2017

Data prima visita nel centro
 10/02/1999

Note

Esordio e Diagnosi

A. Gallo

INNI – Sclerosi Multipla

REGISTRO ITALIANO SCLEROSI MULTIPLA

via esame
ggmmmmmm

Risonanza Magnetica

Tipo di Magnete Utilizzato Area SNC esaminata Somministrazione di Gadolinio Sì No Non so ↻

Informazioni minime obbligatorie - Criteri Mc Donald 2017 DIT

Presenza di Lesioni in T1 Sì No ↻

Presenza di Lesioni in T1 captanti Gadolinio Sì No ↻ Numero di lesioni in T1 captanti Gadolinio Non noto

Presenza di nuove lesioni o di lesioni aumentate di volume in T2 rispetto a RMN precedente Sì No ↻ Numero nuove lesioni o aumentate di volume in T2 Non noto

Numero totale di lesioni in T2 Seleziona...
Seleziona Area SNC per vedere le opzioni

Soddisfatti i Criteri di Mc Donald 2017 per la disseminazione temporale Sì No ↻ [Mostra informazioni](#) [Calcolo automatico](#)

Informazioni aggiuntive - Criteri Mc Donald 2017 DIS

(in riferimento alla area del SNC cervicale e midollo spinale)

Iperintensità in T2 sede corticale/uxtacorticale Iperintensità in T2 sede periventricolare Iperintensità in T2 sede infratentoriale Iperintensità in T2 a carico del midollo spinale

Soddisfatti i Criteri di Mc Donald 2017 per la disseminazione spaziale Sì No ↻ [Mostra informazioni](#) [Calcolo automatico](#)

Allegati

Nessun allegato presente

Carica nuovi allegati Nessun file selezionato

Nota

Inserimento RMN Basale e al Follow-up

A. Gallo

INTEGRAZIONE RISM-RM



- **Obiettivo strategico di FISM e del RISM:**

Integrazione dei dati clinico-demografici-terapeutici del RISM con gli esami RM dei pazienti, al fine di poter svolgere studi retrospettivi e prospettici (di correlazione, monitoraggio e predizione) ancora più accurati e completi.

Questo avanzamento del RISM prevede che i Centri SM possano caricare sulla piattaforma/server del RISM (sempre in maniera criptata) gli esami di RM dei pazienti, laddove vengano richiesti per un progetto del RISM (*) che prevede l'analisi anche dei dati di RM.

Survey conoscitiva sviluppata dai *core centers* di INNI (durata per la compilazione ca. 15 minuti)(**) per "fotografare" le attuali procedure di acquisizione/gestione degli esami RM eseguiti presso i Centri SM partecipanti al RISM.

(*) possibile/da valutare anche, per i Centri SM che lo preferissero, un caricamento dei dati continuo/parallelo all'inserimento dei dati clinici

(**) valutare anche il supporto e la condivisione con un neuroradiologo della struttura a cui afferisce il Centro SM

A. Gallo

Survey RISM-RM (6)

STUDIO ENCEFALO

Linee guida MAGNIMS-CMSC-NAIMS 2021 (requisiti minimi) - Wattjes et al. Lancet Neurology 2021

Raccomandate:

- Immagini T2 (TSE o FSE) assiali con spessore ≤ 3 mm, gap 0 mm e risoluzione sul piano 1x1x1 mm
- Immagini T2-FLAIR sagittali (meglio se 3D T2-FLAIR isotropiche 1x1x1 mm o cmq con spessore sempre ≤ 1.5 mm)
- Immagini T2-FLAIR assiali (**se non disponibile immagini 3D T2-FLAIR sagittali**) con spessore ≤ 3 mm, gap 0 mm
- Immagini T1 assiali post-mdc (oppure 3D sagittali) (raccomandate alla diagnosi; opzionali durante il monitoraggio)

Opzionali:

- Immagini 3D-T1 isotropiche ad alta risoluzione, DWI, DIR, PSIR, SWI

Survey RISM-RM (8)

Quanti esami RM del midollo cervicale di pazienti con SM vengono eseguiti in media ogni anno con questo scanner e con il suddetto protocollo standardizzato? *menù a scelta multipla: <50/anno, 50-100/anno, >100/anno, >200/anno, >500/anno*

Quanti esami RM del midollo cervicale di pazienti con SM sono stati eseguiti fino ad oggi con questo scanner e con il suddetto protocollo standardizzato? *menù a scelta multipla: <50, 50-100, >100, >200, >500*

Quanti degli esami RM del midollo cervicale eseguiti fino ad oggi, con questo scanner e con il suddetto protocollo standardizzato, rispettano i requisiti minimi previsti specificamente dalle recenti linee guida MAGNIMS-CMSC-NAIMS 2021 (riportate di seguito)? *menù a scelta multipla: <50, 50-100, >100, >200, >500, Non so, Altro/Commenti (specificare)*

Linee guida MAGNIMS-CMSC-NAIMS 2021 (requisiti minimi) - Wattjes et al. Lancet Neurology 2021

Raccomandate:

- Almeno 2 immagini/sequenze sagittali tra le seguenti: T2 (TSE o FSE), PD (TSE o FSE) o STIR con spessore ≤ 3 mm, gap 0 mm
- Immagini T1 sagittali dopo contrasto (raccomandate alla diagnosi; opzionali durante il monitoraggio)

Opzionali:

- Immagini T1 sagittali e assiali pre-contrasto, T2 assiali (TSE o FSE), 3D-T1 sagittali (PSIR, FSPGR, MPRAGE)
-

A. Gallo