

# Amyloid Related Imaging Abnormalities

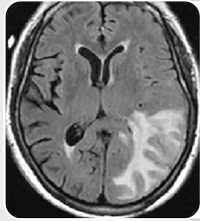
## General Overview for the Radiologist



### ► Amyloid Related Imaging Abnormalities (ARIA)

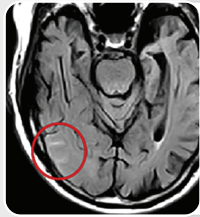
- ▶ A **spectrum of MRI signal abnormalities** associated with **amyloid clearance** in the **brain**<sup>1-3</sup>
- ▶ Can occur spontaneously but more frequently observed during treatment with **amyloid-targeting therapies**<sup>1-3</sup>
- ▶ There are two types of ARIA: **ARIA-E** and **ARIA-H**<sup>2-4</sup>
  - ▶ Both types may be observed on the same scan<sup>5</sup>
  - ▶ ARIA type is determined by nature of **leakage product** and **location**<sup>2,5</sup>
- ▶ **Monoclonal antibodies** directed against aggregated forms of beta amyloid carry a boxed warning regarding the **increased risk for causing ARIA**, which can be serious and life threatening<sup>1-3</sup>
- ▶ **Identification of ARIA** prior to initiation of therapy and ongoing **monitoring via MRI** imaging are crucial during treatment with amyloid-targeting therapies<sup>1-3</sup>

#### Edema<sup>4</sup>



**ARIA-Edema example image:** Hyperintensity on T2 FLAIR in left parieto-occipital lobe, consistent with parenchymal edema

#### Effusion<sup>4</sup>



**ARIA-Effusion example image:** Hyperintensity on T2 FLAIR in the sulci within the right temporo-occipital lobe, consistent with effusion

#### ARIA-E Vasogenic Edema and/or Sulcal Effusion<sup>3-7</sup>

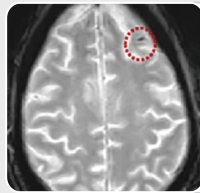
<b>Nature of leakage products</b>	Proteinaceous fluids
<b>Location of increased vascular permeability</b>	Parenchyma: vasogenic edema (parenchymal hyperintensities and gyral swelling)
	Leptomeninges: sulcal effusion/exudate (sulcal hyperintensities)
	Frequently unilateral involving occipital, frontal, and temporal regions
<b>Primary diagnostic imaging sequence</b>	T2 FLAIR
<b>Primary MRI features</b>	T2 FLAIR hyperintense
	DWI negative
	No contrast enhancement
<b>Evaluation of severity</b>	MRI severity scales <sup>7</sup>

#### Microhemorrhage<sup>4</sup>



**ARIA-Microhemorrhage example image:** Punctate foci of signal void on T2\* GRE in an area of parenchymal edema, consistent with microhemorrhage

#### Superficial Siderosis<sup>4</sup>



**ARIA-Siderosis example image:** Signal hypointensity in right temporal area on T2\* GRE, consistent with superficial siderosis on axial

#### ARIA-H Hemosiderin Deposits<sup>3-7</sup>

<b>Nature of leakage products</b>	Blood-degradation products
<b>Location of increased vascular permeability</b>	Parenchyma: microhemorrhage (<10 mm) and intracerebral hemorrhage aka macrohemorrhage (≥10 mm)
	Leptomeninges: superficial hemosiderin deposits (superficial siderosis)
	Frequently develops in the context of ARIA-E
<b>Primary diagnostic imaging sequence</b>	T2* GRE and/or SWI
<b>Primary MRI features</b>	GRE and/or T2* weighted hypointense
	SWI hypointense
<b>Evaluation of severity</b>	Number of microhemorrhages and hemosiderin deposits on MRI

### ► Radiographic Severity Monitoring<sup>5</sup>

	Mild	Moderate	Severe
<b>ARIA-E:</b> Sulcal and/or cortical /subcortical FLAIR hyperintensity Measured in single greatest dimension	1 site <5 cm	1 site 5-10 cm, or >1 site each <10 cm	≥1 site(s) >10 cm
<b>ARIA-H:</b> Number of new* microhemorrhages	≤4	5-9	≥10
<b>ARIA-H:</b> Superficial siderosis	1 focal area	2 focal areas	>2 focal areas

\*New: cumulative number from baseline

Abbreviations: **ARIA-E** = Amyloid Related Imaging Abnormalities-Edema/Effusion; **ARIA-H** = Amyloid Related Imaging Abnormalities-Hemosiderin deposits; **FLAIR** = Fluid-Attenuated Inversion Recovery; **GRE** = Gradient Recalled Echo; **MRI** = Magnetic Resonance Imaging; **SWI** = Susceptibility Weighted Imaging.

1. Salloway S, MD et al. JAMA Neurol. 2022;79:13-21. 2. Filippi M et al. JAMA Neurol. 2022;79:291-304. 3. Sperling RA et al. Alzheimer's Dement. 2011;7:367-385. 4. Figure adapted from Barakos J et al. J Prev Alz Dis. 2022;9:211-220. Copyright © licensed under CC-BY-4.0 (<https://creativecommons.org/licenses/by/4.0/>). Modified from original by cutting.

5. Cogswell PM et al. Am J Neurol. 2022;43:e19-35. 6. Barakos J et al. Am J Neurol. 2013;34:1958-1965. 7. Barkhof F et al. Am J Neurol. 2013;34:1550-1555.

# Amyloid Related Imaging Abnormalities

## ASNR Recommended Reporting Framework



### SPECIFICATIONS

▶ <b>Description</b>	Follow up imaging for patients undergoing treatment with an amyloid-lowering antibody therapy
▶ <b>Examination</b>	MRI of the brain without contrast
▶ <b>History</b>	If information is available: [ <i>Include agents, doses received, date of last dose, and symptoms if present</i> ]
▶ <b>Blood sensitive sequence</b> Potential to use both depending on institution	[ SWI ] or [ GRE/T2* ]
▶ <b>Field strength</b>	[ 3T ] or [ 1.5T ]
▶ <b>Comparison</b>	[ None Available ]



### FINDINGS

#### ▶ Assessment for ARIA-E

▶ <b>Prior FLAIR hyperintensities</b>	[ No prior exam available for adequate comparison ] or [ Yes ] If yes: [ <i>Describe location(s), extent (cm), and change</i> ]
▶ <b>New/incident FLAIR hyperintensities</b>	[ No ] or [ Yes ] [ <i>Describe location(s) and extent (cm)</i> ]
▶ <b>Total current regions of FLAIR hyperintensities</b>	[ None ] or [ 1 ] or [ >1 ]

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Abbreviations: **ARIA-E** = Amyloid Related Imaging Abnormalities-Edema/Effusion; **ARIA-H** = Amyloid Related Imaging Abnormalities-Hemosiderin deposits; **ATT** = Amyloid-Targeting Therapies; **FLAIR** = Fluid-Attenuated Inversion Recovery; **GRE** = Gradient Recalled Echo; **MRI** = Magnetic Resonance Imaging. **SWI** = Susceptibility Weighted Imaging.  
1. ASNR. [https://www.asnr.org/wp-content/uploads/2023/07/AJNR\\_ARIA\\_white\\_paper\\_templates\\_20230713.pdf](https://www.asnr.org/wp-content/uploads/2023/07/AJNR_ARIA_white_paper_templates_20230713.pdf) [Accessed October 2023]. 2. Cogswell PM et al. Am J Neurol. 2022;43:e19-35.

# Amyloid Related Imaging Abnormalities

## ASNR Recommended Reporting Framework



### ► Assessment for ARIA-H

► <b>Microhemorrhages at pre-treatment baseline</b>	[ 0-4 ] or [ 5-9 ] or [ ≥10 ] If present: [ Describe locations, image, and slice number ]
► <b>Prior treatment emergent microhemorrhages</b>	[ No prior treatment monitoring exam available for adequate comparison ] or [ Number of definite microhemorrhages present on prior monitoring exam ] If present: [ Describe locations ]
► <b>New microhemorrhages</b>	[ Number of definite new microhemorrhages since prior exam ] If present: [ Describe locations ]
► <b>Total treatment emergent microhemorrhages = prior treatment emergent + new microhemorrhages</b>	[ 0-4 ] or [ 5-9 ] or [ ≥10 ]
► <b>Prior treatment emergent siderosis</b>	[ No prior exam available for adequate comparison ] or [ Number of prior focal areas of superficial siderosis ]
► <b>New siderosis</b>	[ Number of new focal area of superficial siderosis ]
► <b>Total treatment emergent focal areas of superficial siderosis</b>	[ <1 focal area of superficial siderosis ] or [ <2 focal areas of superficial siderosis ] or [ >2 focal areas of superficial siderosis ]

### ► Impression

Since [ Date of prior ]:  
[ Unchanged ] or [ Increased ] or [ Decreased ] findings of  
[ ARIA-E ] or [ ARIA-H microhemorrhage ] or [ ARIA-H superficial siderosis ]  
most notable in [ Area or areas of the brain with the greatest change ]

Findings for:  
[ No ] or [ Mild ] or [ Moderate ] or [ Severe ] ARIA-E  
[ No ] or [ Mild ] or [ Moderate ] or [ Severe ] ARIA-H microhemorrhages  
[ No ] or [ Mild ] or [ Moderate ] or [ Severe ] ARIA-H related siderosis

# Amyloid Related Imaging Abnormalities

## Monitoring and Management of ARIA

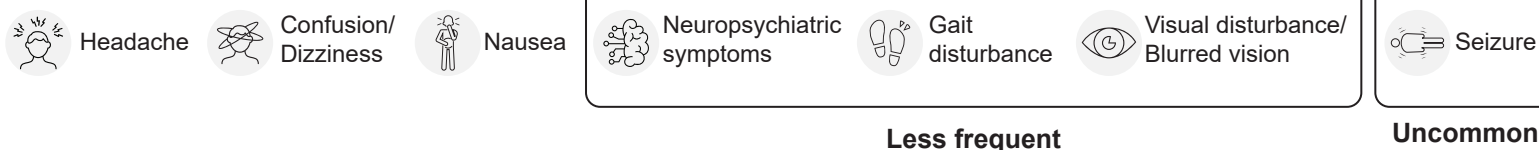


### ► Radiographic Severity Monitoring<sup>1</sup>

	Mild	Moderate	Severe
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### ► Clinical Symptom Severity Monitoring<sup>2-4</sup>



#### Asymptomatic:

No symptoms noted, no disruption of daily activities

#### Mild:

Symptoms noted, no disruption of daily activities

#### Moderate:

Symptoms sufficient to reduce or affect normal daily activities

#### Severe:

Incapacitating with inability to perform normal daily activities

### ► ARIA Monitoring and Management: General Principles<sup>2-4, 5-7</sup>

- ▶ Baseline ARIA evaluation and periodic monitoring with MRI are recommended during treatment with amyloid-targeting therapies
- ▶ Refer to prescribing information for monoclonal antibodies directed against beta amyloid for ARIA monitoring and management guidelines
- ▶ Patients experiencing symptoms suggestive of ARIA should undergo clinical evaluation, including MRI if indicated
- ▶ If ARIA is observed on MRI, careful clinical evaluation should be performed. Dose suspension or discontinuation may be considered based on the presence of symptoms and/or radiographic severity
- ▶ If required, treatment of ARIA revolves around close monitoring of neurologic status and administration of supportive therapy, which may include corticosteroids
- ▶ There is limited experience in patients who continued dosing through ARIA-E
- ▶ There is limited data for dosing patients who experienced recurrent episodes of ARIA-E

Abbreviations: **AD** = Alzheimer's Disease; **ARIA-E** = Amyloid Related Imaging Abnormalities-Edema/Effusion; **ARIA-H** = Amyloid Related Imaging Abnormalities-Hemosiderin deposits; **ATT** = Amyloid-Targeting Therapies; **FLAIR** = Fluid-Attenuated Inversion Recovery; **MRI** = Magnetic Resonance Imaging.

1. Cogswell PM et al. Am J Neurol. 2022;43:e19-35. 2. Cummings J et al. J Prev Alz Dis. 2023;10:362-377. 3. Cummings J et al. J Prev Alz Dis. 2022;9:221-230. 4. Cummings J et al. J Prev Alz Dis. 2021;4:398-410. 5. Salloway S, MD et al. JAMA Neurol. 2022;79:13-21. 6. Filippi M et al. JAMA Neurol. 2022;79:291-304. 7. Sperling RA et al. Alzheimer's Dement. 2011;7:367-385.

# Amyloid Related Imaging Abnormalities

## Detecting ARIA: Recommended MRI Protocol<sup>2</sup>



- ▶ Imaging protocol standardization is necessary to ensure consistent accuracy for diagnosing ARIA, and specific parameters are needed to achieve cross-platform standardization<sup>1</sup>



**3T scanner (recommended),  
1.5T scanner (minimal)**<sup>1,2</sup>

High field scanners have greater sensitivity but limited availability. The use of 1.5T is endorsed as a minimum standard<sup>2</sup>



**Slice thickness<sup>2</sup>: ≤5 mm**

Thinner slices increase resolution but should be balanced against the loss in signal-to-noise ratio<sup>2</sup>



**TE<sup>2</sup>: ≥20 ms**

Longer TE increases sensitivity to detection<sup>2</sup>



**2D T2\* GRE or SWI  
(for ARIA-H)**<sup>2,3</sup>

To identify superficial siderosis and microhemorrhages (ARIA-H) T2\* GRE and SWI MRI sequences are used to improve detection and visualization of microhemorrhages<sup>2</sup>



**T2 FLAIR (for ARIA-E)**<sup>2</sup>

To monitor brain edema or sulcal effusion (ARIA-E)<sup>3</sup>



**DWI**<sup>3</sup>

Recommended for differential diagnosis<sup>3</sup>



**3D T1-GE (optional)**<sup>1</sup>

Anatomical<sup>1</sup>

Abbreviations: **ARIA-E** = Amyloid Related Imaging Abnormalities-Edema/Effusion; **ARIA-H** = Amyloid Related Imaging Abnormalities-Hemosiderin deposits; **DWI** = Diffusion Weighted Imaging; **FLAIR** = Fluid-Attenuated Inversion Recovery; **GRE** = Gradient Recalled Echo; **MRI** = Magnetic Resonance Imaging. **SWI** = Susceptibility Weighted Imaging; **TE** = Time to Echo.

1. Pinter NK et al. Alzheimer's Dement. 2022;18(Suppl. 5):e065547. 2. Cogswell PM et al. Am J Neurol. 2022;43:e19-35. 3. Sperling RA et al. Alzheimer's Dement. 2011;7:367-385. 4. Barakos J et al. J Prev Alz Dis. 2022;9:211-220.