Diagnosis of ARIA

WHAT IS ARIA?

Amyloid-related imaging abnormalities, also known as **'ARIA'**, are a consequence of the presence of amyloid in blood vessel walls (cerebral amyloid angiopathy [CAA]).[1] CAA can cause **spontaneous ARIA** in patients with Alzheimer's disease (AD)[1]

The risk of ARIA is increased with the use of monoclonal antibodies that remove amyloid plaque in patients with AD.[1–3] In these cases, surveillance MRIs can be used to **monitor for ARIA**[1,3]

WHAT ARE THE SYMPTOMS OF ARIA?

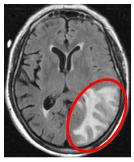
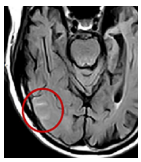
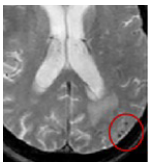
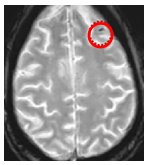
- In most cases, ARIA is found on MRI imaging and is **asymptomatic**[1,4]
- The **symptoms of ARIA-E** are nonspecific and include headache, confusion, nausea, vomiting, visual disturbances, neuropsychiatric symptoms, dizziness, fatigue, or gait disturbances.[1,4,5] **ARIA-H** cases are generally asymptomatic[4]
- Infrequently, **severe neurological symptoms** occur (e.g., encephalopathy, focal neurological symptoms, seizures, and status epilepticus)[4–6]

ARIA MRI FINDINGS INCLUDE[1,2,4]:

- **Parenchymal vasogenic edema** (ARIA-E)
- **Sulcal effusion** (ARIA-E)
- **Superficial siderosis** (ARIA-H)
- **Cerebral microhemorrhages** (ARIA-H)
- **Intracerebral hemorrhage** (also termed macrohemorrhages)

ARIA-E AND ARIA-H[4]

ARIA is subdivided into **ARIA-E** (edema/sulcal effusion) or **ARIA-H** (hemosiderin/hemorrhage)[4]
ARIA-E and H may occur concurrently[2]

	ARIA-E	ARIA-H
Primary diagnostic **imaging sequence**	**T2-FLAIR**[2]  edema  effusion	**T2*GRE**[2]  microhemorrhage  superficial siderosis
Image findings	**Increased signal** on FLAIR images, no abnormal diffusion restrictions[2]	**Very-low-intensity signals** on T2*GRE MRI images[1,4]
Nature of leakage products	Proteinaceous fluids[4]	Blood-degradation products[4]
Location of increased vascular permeability	**Parenchyma:** vasogenic edema[4] **Leptomeninges:** sulcal effusions (i.e., exudates)[4]	**Parenchyma**: microhemorrhages (<10 mm) and intracerebral hemorrhage (also termed macrohemorrhages) (≥10 mm) **Leptomeninges:** superficial hemosiderin deposits (superficial siderosis)[4]
Evaluation of **severity**	**Symptoms** and **MRI severity scales**[4,7]	Assessment of **symptoms** and number of **microhemorrhages and hemosiderin deposits** on MRI[4,7]

MRI images from Barakos et al (2022)

AVOIDING PITFALLS FOR DETERMINING RADIOGRAPHIC SEVERITY

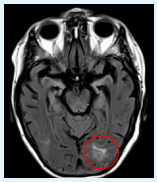
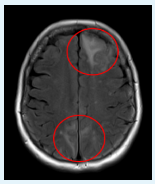
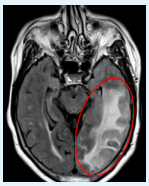
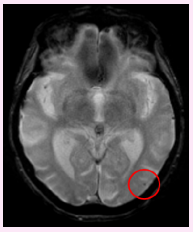
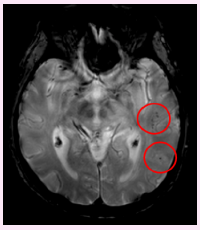
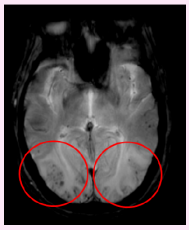
ARIA-E can be easily missed by conventional T2 sequence due to the T2 hyperintensity of CSF, justifying the need for a T2-FLAIR sequence[2]

ARIA-E: avoid imaging patients on different scanners over time since white matter signal may differ with scan technique and field strength; identification of shading artifacts may also be difficult owing to scanner or sequence variability[7]

ARIA-H: susceptibility weighted imaging (SWI) is more sensitive for the detection of microhemorrhages versus T2*GRE images[1]

ARIA SEVERITY RADIOGRAPHIC GRADING

ARIA-E, ARIA-H microhemorrhage, and ARIA-H superficial siderosis are each categorized by radiographic severity (mild to severe) based on the following criteria[7]

	MILD	MODERATE	SEVERE
ARIA-E Sulcal and/or cortical/subcortical FLAIR hyperintensity	1 location <5 cm 	1 location 5–10 cm **OR** >1 location each <10 cm 	≥1 location >10 cm 
ARIA-H Superficial siderosis	1 focal area	2 focal areas	>2 focal areas
ARIA-H Number of new microhemorrhages	≤4 treatment-emergent microhemorrhages 	5–9 treatment-emergent microhemorrhages 	≥10 treatment-emergent microhemorrhages 

ARIA is graded on the basis of treatment-emergent events. For ARIA-H, this count includes cumulative new microhemorrhages or regions of siderosis compared with the baseline, pretreatment examination.[7] MRI images data on file

MRI ACQUISITION PROTOCOLS TO DETECT AND MONITOR ARIA[1,3]

MRI protocol: standards for detection of ARIA in clinical trials

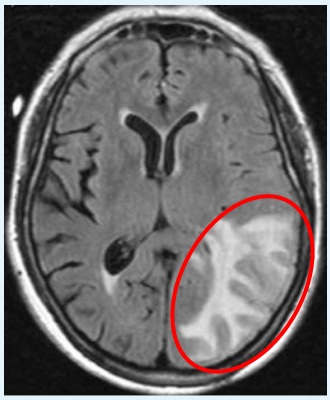


Figure adapted from Barakos et al (2022)

3T scanner (recommended) 1.5T scanner (minimal)[1,7]	High-field-strength scanners have greater sensitivity but limited availability. The use of 1.5T scanner is endorsed as a minimum standard[1]
Slice thickness[1]: ≤5 mm	Thinner slices increase resolution, but decrease signal-to-noise ratio[1]
TE[1]≥20 ms	Longer TE increases sensitivity to detection[1]
2D T2*GRE or SWI (for ARIA-H)[1,3]	To identify superficial siderosis and microhemorrhages (ARIA-H),[1] T2*GRE and SWI are MRI sequences used to improve the detection and visualization of microhemorrhages[1]
T2-FLAIR (for ARIA-E)[1]	To monitor brain edema or sulcal effusion (ARIA-E)[3]
Diffusion weighted imaging **(DWI)**[3]	Recommended for differential diagnosis[3]

REFERENCES:

1. Sperling RA, et al. Alzheimers Dement. 2011;7(4):367–385;
2. Barakos J, et al. AJNR Am J Neuroradiol. 2013;34(10):1958–1965;
3. Barakos J, et al. J Prev Alzheimers Dis. 2022;9(2):211–220;
4. Filippi M, et al. JAMA Neurol. 2022;79(3):291–304;
5. Salloway S, et al. JAMA Neurol. 2022;79(1):13–21;
6. VandeVrede L, et al. Alzheimers Dement (Amst). 2020;12(1):e12101;
7. Cogswell PM, et al. AJNR Am J Neuroradiol. 2022;43(9):E19–E35.

ABBREVIATIONS:

AD, Alzheimer's disease; ARIA, amyloid-related imaging abnormalities (includes ARIA-E and H); ARIA-E, ARIA-edema/effusion; ARIA-H, ARIA-hemosiderin/hemorrhage; CAA, cerebral amyloid angiopathy; CSF, cerebrospinal fluid; DWI, diffusion weighted imaging; FLAIR, fluid-attenuated inversion recovery; GRE, gradient recalled echo; MRI, magnetic resonance imaging; SWI, susceptibility weighted imaging; T, Tesla; TE, echo time.

For additional information on ARIA, scan here:

www.UnderstandingARIA.com

Eisai hhc human health care