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**[1,31]

There are two subtypes of ARIA: **ARIA-E** where the imaging findings are related to edema or effusions and **ARIA-H**, where the imaging findings are related to hemorrhage or hemosiderin deposition

WHAT ARE THE SYMPTOMS OF ARIA?

In most cases, ARIA is found on routine, monitoring 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]

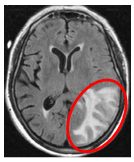
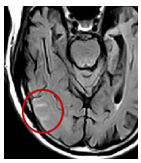
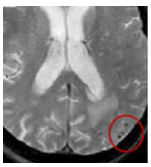
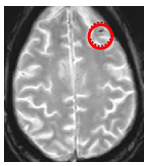
ARIA can be serious and life-threatening[7]

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 restricted diffusion[2]	**Very-low-intensity signals** on T2*GRE MRI images[1,4]
Nature of leakage products	Proteinaceous fluid[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**	**Size** and number of **separate locations**	Number of **microhemorrhages** and **number of areas of superficial siderosis**

MRI images from Barakos et al (2022)

AVOIDING PITFALLS FOR DETERMINING RADIOGRAPHIC SEVERITY

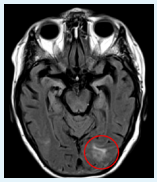
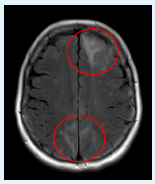
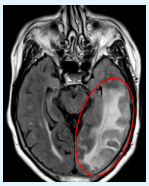
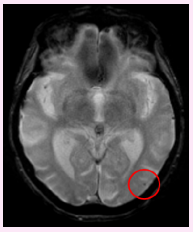
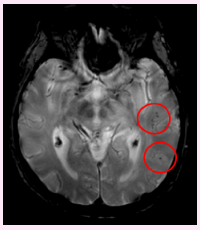
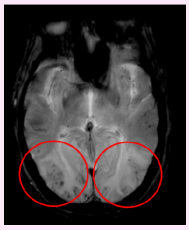
ARIA-E can be easily missed by conventional T2 sequence due to the T2 hyperintensity of CSF, justifying the need for a T2-FLAIR sequence[2]

Best practice for baseline imaging and monitoring is to scan the patient at the same field strength (1.5 or 3T), using the same technique (sequences, acquisition parameters and angle), and preferably with the same scanner for the patient.

Either SWI (susceptibility weighted imaging) or GRE(gradient echo) imaging are acceptable. SWI is more sensitive for detecting microhemorrhages and blood products, but clinical trials, to date, have used T2*/GRE sequences for patient inclusion/exclusion and monitoring.

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

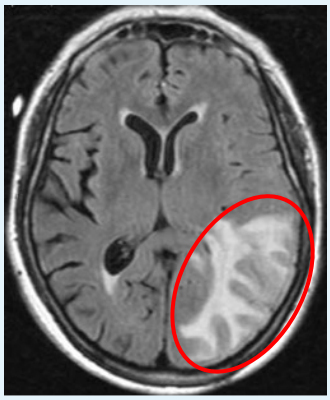


Figure adapted from Barakos et al (2022)

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 on GRE increases sensitivity for hemorrhage 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.ca

Eisai hhc human health care