

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.^{5,6} **ARIA-H** cases are generally asymptomatic⁴
- Infrequently, **severe neurological symptoms** occur (e.g., encephalopathy, focal neurological symptoms, seizures, and status epilepticus)⁵⁻⁷

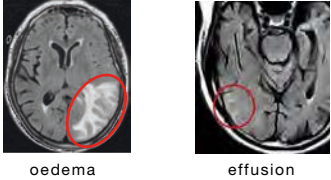
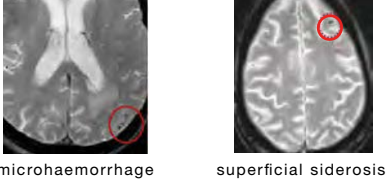


ARIA MRI FINDINGS INCLUDE¹⁻³:

- **Parenchymal vasogenic oedema** (ARIA-E)
- **Sulcal effusion** (ARIA-E)
- **Superficial siderosis** (ARIA-H)
- **Cerebral microhaemorrhages** (ARIA-H)
- **Intracerebral haemorrhage** (also termed macrohaemorrhages)

ARIA-E AND ARIA-H

ARIA is subdivided into **ARIA-E** (oedema/sulcal effusion) or **ARIA-H** (haemosiderin/haemorrhage)⁴
ARIA-E and ARIA-H may occur concurrently²

	ARIA-E	ARIA-H
Primary diagnostic imaging sequence	T2-FLAIR ² 	T2*GRE ² 
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 oedema ⁴ Leptomeninges: sulcal effusions (i.e., exudates) ⁴	Parenchyma: microhaemorrhages (<10 mm) and intracerebral haemorrhage (also termed macrohaemorrhages) (≥10 mm) Leptomeninges: superficial haemosiderin deposits (superficial siderosis) ⁴
Evaluation of severity	Symptoms and MRI severity scales ^{4,8}	Assessment of symptoms and number of microhaemorrhages and haemosiderin deposits on MRI ^{4,8}

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AVOIDING PITFALLS FOR DETERMINING RADIOGRAPHIC SEVERITY



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



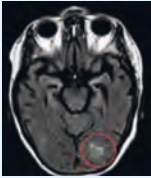
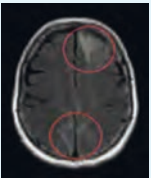

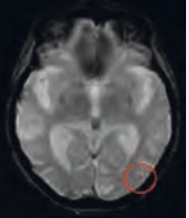
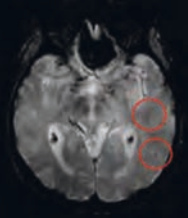

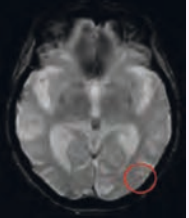
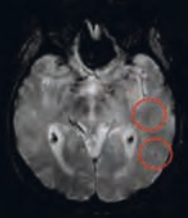

ARIA-E: avoid imaging patients on different scanners over time since white matter signal may differ with scan technique and field strength; identification of shading artifacts may also be difficult owing to scanner or sequence variability⁸



ARIA-H: **susceptibility weighted imaging** (SWI) is more sensitive for the detection of microhaemorrhages versus T2*GRE images¹

ARIA SEVERITY RADIOGRAPHIC GRADING

ARIA-E, ARIA-H microhaemorrhage, and ARIA-H superficial siderosis are each categorised by radiographic severity (mild to severe) based on the following criteria⁸

	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 microhaemorrhages	≤4 treatment-emergent microhaemorrhages 	5–9 treatment-emergent microhaemorrhages 	≥10 treatment-emergent microhaemorrhages 

ARIA is graded on the basis of treatment-emergent events. For ARIA-H, this count includes cumulative new microhaemorrhages or regions of siderosis compared with the baseline, pretreatment examination.⁸ Eisai internal MRI images

MRI ACQUISITION PROTOCOLS TO DETECT AND MONITOR ARIA^{1,3}

MRI protocol: standards for detection of ARIA in clinical trials

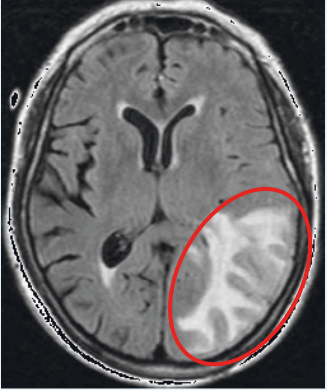


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3T scanner (recommended) 1.5T scanner (minimal)^{1,8}	High-field-strength scanners have greater sensitivity but limited availability. The use of 1.5T scanner is endorsed as a minimum standard ¹
Slice thickness¹: ≤5 mm	Thinner slices increase resolution, but decrease signal-to-noise ratio ¹
TE¹: ≥20 ms	Longer TE increases sensitivity to detection ¹
2D T2*GRE or SWI (for ARIA-H)^{1,3}	To identify superficial siderosis and microhaemorrhages (ARIA-H), T2*GRE and SWI are MRI sequences used to improve the detection and visualisation of microhaemorrhages ¹
T2-FLAIR (for ARIA-E)¹	To monitor brain oedema or sulcal effusion (ARIA-E) ³
Diffusion weighted imaging (DWI)³	Recommended for differential diagnosis ³

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Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il> or emailed the registration holder's safety unit at: eir_pv@eisai.net

For medical education purposes. This material is intended to provide an overview of ARIA diagnosis based on available literature

ABBREVIATIONS:

AD, Alzheimer's disease; ARIA, amyloid-related imaging abnormalities (includes ARIA-E and H); ARIA-E, ARIA-oedema/effusion; ARIA-H, ARIA-haemosiderin/haemorrhage; 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 full information please refer to LEQEMBI SPC as approved by the Israeli MOH.