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Spot the Signal: Global Radiology Training for ARIA Detection in Alzheimer's Care

What Are Amyloid-Related Imaging Abnormalities (ARIA)?

Dr. Benzinger:

First and foremost, what are ARIA? The most important word is imaging, meaning that these are findings seen on brain MRIs in patients undergoing new treatments for AD.¹

The ATTs, lecanemab and donanemab, are monoclonal antibody infusions used in the early stages of AD.^{2,3} Routine MRIs are performed before treatment initiation and during the course of treatment with these agents, meaning that these are typically ordered in asymptomatic patients. Quite common adverse events include what we call ARIA-E, vasogenic edema or sulcal effusions that can show up on fluid-attenuated inversion recovery (FLAIR), and ARIA-H, meaning microhemorrhages and superficial siderosis.¹ Radiologists are very familiar with these features because they look very much like what we know as cerebral amyloid angiopathy (CAA). For patients on ATT, it is vitally important to identify these imaging findings as soon as possible within the MRI monitoring schedule because they change the clinical management of the patient.

Predictors for ARIA are generally the same as predictors for CAA, which are APOE4 genotype or evidence of prior hemorrhages, so the baseline microhemorrhages and siderosis give us a sense that a patient may have preexisting vascular amyloid, making it potentially dangerous for them to be treated with ATTs for AD.

When symptoms are seen with ARIA, they are often nonspecific and can include headache, confusion, visual changes, dizziness, and sometimes nausea or gait difficulty. ARIA are rarely serious; fewer than 2% of patients progress to more serious manifestations, which would include seizures, encephalopathy, hospitalization, or neurologic deficits. However, it is extremely important for us as radiologists to detect ARIA on the imaging as early as possible so that the patient's symptoms can be assessed and the therapies can be paused in order to prevent progression.

To emphasize this point, it is vitally important for the radiologist to identify ARIA on the images rather than to assume that someone else will make that diagnosis.

Dr. Lövblad:

The European Medicines Agency has also authorized these 2 ATTs for the treatment of early AD, first lecanemab in May 2025 and then donanemab in October 2025.^{4,5} However, implementation of these therapies is still in the very early stages in many countries. For example, donanemab has only recently been authorized in Switzerland, and additional therapies are anticipated. In Europe, we are truly at the very beginning of implementation and so we can learn and benefit from the experience that US radiologists have already acquired in the time since the approvals in your country.

The indications in Europe basically mirror those in the United States, being patients who have mild cognitive impairment or mild dementia due to AD with confirmed amyloid pathology. One notable difference from the United States is that, at least initially, treatment will be limited to APOE4 noncarriers or heterozygotes. This approach narrows the eligible population during the early implementation phase. The monitoring schedule is basically also the same as that of the United States, and much of the work we have done in the

various medical societies has been based on the existing American recommendations.

ALZ-NET Real-world ARIA Rates

Dr. Benzinger:

Real-world data suggest that approximately 20% of ARIA cases will be asymptomatic, which is important to recognize.⁶ If you read 5 of these scans in a week, you should see 1 case of ARIA. It is not a rare occurrence but a rather common finding to see on a routine MRI for a patient treated with ATT. Radiologists who interpret MRIs for several patients treated with ATTs should expect to encounter ARIA relatively frequently, rather than viewing it as a rare complication.

Recognizing how common ARIA is in treated populations helps set expectations for radiologists and other healthcare professionals (HCPs) on the care team and reinforces the need for careful, systematic review of both eligibility and monitoring scans.

MRI Monitoring Schedule for ATTs

Dr. Benzinger:

The 2 available ATTs, donanemab and lecanemab, have slightly different dosing regimens and also slightly different MRI schedules to monitor for ARIA.^{7,8} Typically, MRIs are scheduled at baseline (before the first infusion) and at multiple time points during treatment, which are often preplanned at the time of patient enrollment to start therapy. If we see a positive finding on any MRI, then we recommend additional scans for follow-up 1 or 2 months after that positive MRI until edema (for cases of ARIA-E) has completely resolved and/or hemorrhages (for cases of ARIA-H) have stabilized. Clearly, this is a substantial number of scans for the patients and additional workload for radiology practices.

American Society for Neuroradiology (ASNR)

Dr. Benzinger:

There are some key reference guidelines radiologists can use to make sure that scans are being done correctly. The ASNR and related professional societies have developed detailed technical guidelines for ARIA monitoring.^{9,10} The key principle is consistency; scans should be performed using standardized protocols to allow reliable comparison over time.

If you go to the ASNR website, for example, you will find links to download vendor-specific protocols for Siemens, GE, and Philips scanners, so you don't have to build the protocols from scratch yourself.¹¹ Adherence to these protocols supports reproducible detection of subtle ARIA findings and reduces inter-reader variability.

I want to add a little color to some details here, too. The question of SWI vs T2 comes up in nearly every conversation with radiologists. A related issue is field strength: 1.5 vs 3 Tesla (3T). For those outside neuroradiology, it may seem logical to think 3T SWI is always best, but in practice, it is not that straightforward. Because of advances in gradients, coils, software, and pulse sequences, higher field strength does not automatically mean better imaging. If I compare my oldest 3T scanner with my newest 1.5T scanner, I can often obtain better brain images from the newer 1.5T system.

In my experience, consistency is the most important factor. If a patient can remain on the same scanner over time, that provides the best longitudinal comparison. However, most of us do not practice in that kind of environment. In my health system alone, we have 60 MRI scanners serving patients across a 300-mile radius, so it is simply not feasible for every patient to return to the same scanner each time.

I do typically begin with 3T using both SWI and GRE. This gives a baseline sense of where hemorrhages are and what they look like as a grounding point for future comparisons. We are sometimes asked why we continue to acquire both sequences on follow-up. One key reason is motion. SWI is highly sensitive and excellent for detecting small findings, but only if the patient can remain still. It is important to remember that patients with dementia, particularly those experiencing ARIA symptoms, often have difficulty tolerating an MRI exam. SWI may fail entirely because of motion. In those situations, the faster GRE/T2* sequence can "save the day" and still allow us to identify critical findings. This is why, in our practice, we obtain both.

Using the ASNR protocols, we have streamlined our monitoring exams. We only acquire FLAIR, GRE, SWI, and DWI. We do not routinely obtain T1, T2, arterial spin labeling, or additional sequences. As a result, our monitoring exam takes about 10 minutes from start to finish. When I interpret the study, I focus only on those essential images. The findings can be subtle, so they require careful review, but they are not buried in thousands of unnecessary images. That is the philosophy guiding our approach.

Dr. Lövblad:

This is exactly why we recommend limiting the exam to 4 or 5 sequences at most. Time matters, and patient tolerance matters. As noted, many of these patients cannot remain in the scanner for 30 minutes. The shorter we can make the exam, the better.

Swiss Society for Neuroradiology (SSNR) Recommendations

Dr. Lövblad:

Recommendations from the SSNR are almost identical to those proposed by the ASNR, with gradient echo (GRE) and susceptibility-weighted (SWI) images to detect microhemorrhages.^{10,11} Using both sequences is particularly helpful. Diffusion-weighted imaging (DWI) is valuable for identifying alternative pathologies such as stroke, particularly when patients come in urgently. FLAIR imaging is used to look for the presence of hyperintensities that enter the white matter or infarcts that might be older and not necessarily detected by DWI. Baseline examinations follow standard reporting protocols, whereas follow-up reporting differs depending on whether patients are asymptomatic or symptomatic.

In asymptomatic patients, we will not use IV contrast, but we find it may be useful in symptomatic patients, and we perform the combination of the 4 basic sequences or 5, including DWI, GRE, SWI, T2, and 3D imaging. Everything is considered on a case-by-case basis, and depending on grading, additional sequences may be ordered. Communication of findings is essential so that treating HCPs can make clinical treatment decisions, which may be more cautious in some circumstances.

Management of ARIA With ATTs

Dr. Benzinger:

When an MRI finding of ARIA-E or H is detected, that triggers the start of a treatment algorithm. The next step is correlation with symptoms. A positive or worsening case of ARIA necessitates a call to the referring physician's office so that they can get in touch with the patient and assess whether symptoms are present, if that is known.

Treatment is then guided by the ARIA severity as determined by standardized grading. For severe ARIA, treatment is stopped regardless of the presence or absence of symptoms. If the patient has mild or moderate ARIA with symptoms, they go down 1 side of this flowchart. If they are asymptomatic, the treatment differs for mild vs moderate ARIA. This demonstrates the importance of the radiologist applying the correct grading scale to the images. The terms mild, moderate, and severe here are not subjective measures ("oh, it looks pretty bad to me"). A standardized objective severity scale is used across all the ATTs to drive clinical management decisions.

Dr. Lövblad:

As noted previously, ideally, scans should be done on the same scanner at the same field strength. That might not always be possible because sometimes patients go to clinics or hospitals other than the one where they were initially treated. Maximal standardization is recommended, as comparison with prior studies is frequently essential. If different scanners or protocols are used, ARIA detection and evaluation can be difficult even for radiologists specifically trained in this area. Appropriate scans include FLAIR for edema in ARIA-E and some type of SWI T2* images for hemorrhage in ARIA-H.

Dr. Benzinger:

For ARIA-E, grading is based primarily on the number and size of involved regions on FLAIR. For ARIA-H, separate grading criteria exist for microhemorrhages and for superficial siderosis, largely based on lesion count. Management options range from continued treatment with routine monitoring to temporary suspension of therapy, enhanced MRI surveillance, dose modification, or permanent discontinuation, depending on ARIA severity and the presence or absence of symptoms.^{3,4,7,8}

From the radiology perspective, it is essential not only to identify ARIA but also to apply the correct grading criteria in the report and explicitly recommend follow-up imaging when appropriate, as these elements directly influence clinical decision-making.

Case 1: Eligibility and Baseline Assessment

Dr. Benzinger:

In this case, an 83-year-old woman presented with memory loss. She lived alone in a freestanding house and remained independent in activities of daily living (ADLs), including cooking, shopping, and laundry. Her Mini-Mental State Exam (MMSE) score was 27/30, and her Clinical Dementia Rating (CDR) was 0.5, both of which indicate questionable to very mild cognitive impairment, so this patient is very early in the disease process.¹² The information about her ADLs and living independently is also a component of the CDR. For many families, the goal of therapy is maintaining independence as this patient currently is, so enabling her to continue for as long as possible would be important.

The other important features include current medications, particularly anticoagulants or antiplatelets, since these will further increase risk for hemorrhages, and APOE genotype. The APOE4 variant is associated with a higher risk of ARIA, and in some places, including

in the Veterans Administration system in the United States, homozygous APOE4 carriers may not be eligible for ATT because of the increased vascular amyloid risk.

Dr. Lövblad:

As mentioned above, it is also the case in Europe that homozygous APOE4 carriers are not eligible for ATTs according to regulatory indications.

Case 1: Baseline Imaging

Dr. Benzinger:

This is an example of a positive amyloid PET scan. There is very little uptake in the cerebellar cortex, but a lot of uptake in the white matter and in the gray matter. This would therefore be considered positive for amyloid pathology characteristic of AD.

Her brain MRI is mostly normal, except for relatively small temporal lobes and hippocampi. We are used to thinking about AD MRIs as having a lot of atrophy, so when we see a scan like this, we might initially think the patient does not have AD because the volume looks almost normal. We need to remember that the ATTs are used to treat patients at such an early stage of disease that only subtle changes might be present.

Dr. Lövblad:

This represents a new paradigm for radiologists to see AD looking a little bit different from what we are used to, because we are now looking for and identifying it very early on.

Case 1: Baseline MRI

Dr. Benzinger:

This patient's baseline MRI images do not show any microhemorrhages on SWI or GRE/T2*. Clinical trials were performed with T2*, but in most cases SWI has more sensitivity for small microhemorrhages. We perform both the SWI and the GRE/T2* routinely at our institution, because this helps calibrate what is seen in practice to what we know about from clinical trials and maximize findings.

FLAIR images reveal essentially a very close to normal FLAIR examination, potentially with some mild white matter hyperintensities, but not severe, and no signs of a prior infarct or other abnormality. Important things that we want to report on the baseline MRI include no microhemorrhages, no siderosis, no infarcts, and no other structural abnormalities.

Case 1: ATT Monitoring MRI

Dr. Benzinger:

This patient started receiving ATT therapy, and these are routine monitoring images before an infusion. The top row is the current exam; the bottom row is her prior exam. Arrows have been placed to clarify areas of interest.

Case 1: Detection of ARIA-E

Dr. Lövblad:

The prior MRI, which is in the lower row, is normal. With the help of the arrows, it is very clear on the follow-up scans that now there are ARIA-E both frontally and in the occipital region. The next step would then be to grade it and determine whether the patient has symptoms.

Dr. Benzinger:

This is the tricky part because overall, we might think it looks mild. But in fact, if you have 2 separate regions of the brain, as in this case, frontal and occipital, automatically it becomes moderate according to the grading classification.

This example illustrates that visual impression alone may be misleading; radiologists must apply the formal grading scale rather than relying on subjective assessments of what appears "mild" or "moderate."

Case 1: Detection of ARIA-H

Dr. Benzinger:

SWI in the same regions as the ARIA-E demonstrated 3 microhemorrhages in the right frontal lobe and 1 microhemorrhage in the right occipital lobe, consistent with ARIA-H. As is often the case, ARIA-H lesions appeared in the same locations as ARIA-E, although in some patients either the edema or the hemorrhagic component may be easier to recognize.

Case 1: ARIA Grading Criteria

Dr. Benzinger:

Applying the ARIA grading scale in practice is not always intuitive and can be challenging even for those who use it regularly. A radiologist's role is to identify and quantify findings. I would recommend building some solid reporting templates so that if you click the number of microhemorrhages, the template will automatically give you the grade, so that is 1 less thing you have to keep in your mind in real time. In this case, there were 4 new microhemorrhages, so even though it might have looked concerning since they were located in 2 different parts of the brain, the ARIA-H would be classified as mild. The reverse is true for the siderosis; on FLAIR, it would be considered moderate, because even though they were small regions, 2 different regions were involved.

For **ARIA-E**, grading is based on both size and distribution:

- **Mild:** A single region <5 cm
- **Moderate:** 2 or more regions, or any region measuring 5-10 cm
- **Severe:** Any region ≥10 cm

For **ARIA-H microhemorrhages**, grading is strictly numerical. Location and clustering do not change the category:

- **Mild:** Fewer than 5
- **Moderate:** 5-9
- **Severe:** ≥10

ARIA-H superficial siderosis (a sign of small subarachnoid hemorrhage) follows a tighter scale:

- **Mild:** 1 focus (new or worsening area)
- **Moderate:** 2 foci
- **Severe:** ≥3 foci

The key takeaway is that ARIA assessment is a combination of 2 elements:

1. Imaging severity based on MRI findings
2. Clinical symptom severity

Both must be considered together when determining management.^{3,4} This case is a nice example of moderate ARIA-E and mild ARIA-H, with the findings both occurring in the same regions.

Case 1: ARIA-H Management

Dr. Benzinger:

This case was mild ARIA-H, so clinical management (the decision to suspend dosing) will depend upon whether this patient is having symptoms.

Management decisions depend on both radiologic severity and clinical symptoms. Options include continued treatment with closer monitoring, temporary suspension of therapy until findings resolve or stabilize, dose adjustment, or permanent discontinuation.^{3,4} Radiologists should clearly report the ARIA grade and recommend follow-up MRI, recognizing that treating HCPs may choose a more conservative approach than the minimum required by the product labeling.

Case 1: ARIA-E Management

Dr. Benzinger:

Radiology would definitely recommend that the patient get a follow-up MRI to make sure that the ARIA-E resolves over time, which we would expect. We also expect that those hemorrhages should stabilize, and we should not see new ones. If new hemorrhages appear, we need to continue monitoring with MRI more frequently than the normally indicated schedule.

Case 1: Summary and Key Takeaways

Dr. Benzinger:

This case has several take-home messages.

This patient did have 1 APOE4 allele, so we know from the outset that they have a higher risk for ARIA than the general population.

This case provides a great example of how scoring systems may not align with a radiologist's intuitive sense of lesion severity. It further

emphasizes the importance of applying standardized grading systems since the identification and grading by the radiologist drives clinical management.

In addition, radiology should be vocal in recommending follow-up scans even when therapy is paused because patients are still at risk for progression even if they don't continue to receive the ATT.

In this case, the patient was asymptomatic, but the clinical team decided to hold the infusion because of the involvement of 2 separate areas, both of which included hemorrhages. This illustrates that management may be individualized and more cautious than labeling alone might suggest.

Case 2: Eligibility

Dr. Benzinger:

Our next case is more straightforward than the first one. This is a 74-year-old male reporting gradual-onset memory loss. He lives at home with his spouse, performs home repairs, recently installed a new thermostat, and drives independently. His MMSE was 23/30, so a bit more advanced than in the first case, but still in the reasonable range for therapy, and his CDR is 0.5. His medications do not include any anticoagulants, but he does take 81 mg of aspirin per day. He is also an APOE4 heterozygous carrier, so he has 1 APOE4 allele. He had an amyloid PET scan with florbetapir, which was positive with uptake in the cortex and sparing in the cerebellum.

A key clinical factor is that he is living very independently right now. His symptoms are mild. He is biomarker positive for amyloid, which is required for ATT. He has a mildly elevated risk for ARIA because of his 1 APOE4 allele. He does have an antiplatelet medication on board, but in the US, taking aspirin is allowed with these therapies.

Case 2: Baseline Imaging

Dr. Benzinger:

Brain volumetrics are normal, and in fact, hippocampal volumes are actually better than normal with no atrophy.

Title: Case 2: Baseline MRI

Dr. Benzinger:

This is another case in which the brain MRI appears almost normal; FLAIR, SWI, and GRE/T2* all look very good. An astute observer might note a prior burr hole, prompting clarification regarding the reason for his previous craniotomy.

Case 2: ARIA Detection

Dr. Benzinger:

After ATT was initiated, monitoring MRI revealed new FLAIR hyperintensity involving a single, relatively large region (>9 cm) with sulcal effacement and subtle sulcal effusions, consistent with ARIA-E.

Case 2: ARIA Detection (Detail)

Dr. Benzinger:

In the same region, SWI demonstrated signal loss compatible with superficial siderosis. Without careful comparison to the prior study, these findings could easily be overlooked.

Case 2: ARIA Classification

Dr. Benzinger:

Regarding ARIA classification, we have a single region measuring over 9 cm on FLAIR, and upon careful inspection, effacement of the sulci and even some small sulcal effusions can be seen. In those same ARIA regions that have the sulcal effusions, there is a loss of signal on susceptibility, indicating a little bit of siderosis starting. The FLAIR abnormality is classified as moderate because it is less than 10 cm. However, 3 areas of siderosis place this in the severe ARIA-H category.

Case 2: Potential Pitfalls of Head CT

Dr. Benzinger:

This case was initially interpreted by a radiologist less familiar with ARIA, and in fact, they saw the siderosis and sulcal effusions, and thinking this patient could have a subarachnoid hemorrhage, decided to order a head computed tomography (CT).

A head CT is not required when these findings are recognized as a classic presentation for ARIA. The appropriate step is to notify the referring HCP to assess symptoms and use the symptomatology to apply the grading scale accurately and help guide management.

On careful inspection, that same sulcal effusion seen on MRI is showing up as just a little bit of gray area in the sulcus on the head CT as well.

Dr. Lövblad:

It is also an important point that if the blood is not entirely fresh, it might not show up as well on a CT as on the combined MRI sequences, and this is very important.

Dr. Benzinger:

In fact, if a patient comes to the emergency room with a headache or other symptoms of ARIA, many ERs are not set up to perform an MRI, but if you got only the head CT, you would miss the finding. It is important to recognize that MRI sequences are the appropriate studies for patients receiving ATT.

Case 2: Lessons Learned

Dr. Benzinger:

The key lesson from this case is the routine recognition of the appearance of ARIA. Without a full clinical history, ARIA should be considered in all older patients, given the prevalence of AD. Another lesson is that a head CT or a CT angiography (CTA) is not needed in these cases.

In our system, we have built out nice templates for reporting these examinations that come up automatically for us, so that if you just click 3 for siderosis, it will report severe ARIA-H. –But if the template is modified or the wrong template is loaded, then the reading radiologist will come to the wrong conclusion. This is an important operational lesson to keep in mind.

In this case, the optimal radiology response would have been to recognize the imaging pattern as characteristic of ARIA, assign the appropriate severity grade, and communicate the findings promptly to the referring HCP for clinical correlation, rather than defaulting to CT for evaluation of possible hemorrhage.

This illustrates 2 key points:

1. ARIA is best evaluated with MRI; CT and CTA are not required for typical ARIA presentations and may fail to demonstrate the relevant abnormalities.

When a patient known to be receiving ATT presents to the emergency department with symptoms such as headache, ARIA should be suspected and MRI, including FLAIR and SWI, should be ordered.

Case 3: Subtle ARIA and Retrospective Detection

Dr. Benzinger:

This case represents a new patient on ATT. As with the other cases, we have a FLAIR, an SWI, and a GRE/T2*. The findings here are very subtle.

Case 3: Subtle ARIA (Detail)

Dr. Benzinger:

Consider the image in the middle on the bottom, circled in red. In the left frontal lobe, subtle darkness or loss of signal can be seen, which is new compared with baseline imaging. On careful review, it is associated with a very subtle effusion and edema. This ARIA-E was missed on the middle monitoring visit.

Case 3: Subtle ARIA (Grading)

Dr. Benzinger:

The patient developed siderosis at the same location which was identified at the next follow-up, prompting retrospective review and recognition of the subtle abnormality on the prior study. In this case, he had mild ARIA-E on the prior visit and then developed mild ARIA-H as well.

Case 3: Lessons Learned

Dr. Benzinger:

Radiologists may have cases where ARIA is identified in retrospect; it is important to communicate these findings to the clinical team about increased risk for future episodes. Because changes may be incremental over time, it is essential to review not only the most recent prior study but also the baseline examination, even when multiple time points are available.

If a prior report described the study as normal, that does not necessarily mean no abnormality was present; careful independent review remains essential. Radiologists should maintain a high index of suspicion; if ARIA is not being detected at a rate consistent with expectations (eg, approximately one case per five treated-patient MRIs), it is likely being under-recognized.

Case 4: Moderate ARIA-E and ARIA-H

Dr. Benzinger:

This is a nice example of edema and effusions on FLAIR having similar findings on SWI for siderosis.

Case 4: Moderate ARIA-E and ARIA-H (Detail)

Dr. Benzinger:

Purple arrows in the inset images show areas of interest; again, the 2 findings occur in the same brain regions.

Case 4: Moderate ARIA-E and ARIA-H (Grading)

Dr. Benzinger:

Classification for ARIA-E will be moderate because there were 2 different regions less than 10 cm each. For ARIA-H, there were 2 regions of siderosis, so that classification is moderate as well. Our actions would include notifying the clinical team, documenting the grading in our report, and recommending a follow-up MRI for stabilization vs progression. The clinical team will correlate symptoms and determine whether therapy should be paused under the treatment algorithm. Once a case falls into the moderate range, therapy would typically be paused until ARIA resolves/stabilizes.

Case 4: Lessons Learned

Dr. Benzinger:

This case serves as a reminder of the importance of communication among the healthcare team, particularly from the radiologist when pausing treatment might be in the patient's best interest. This case also illustrates that when edema is visible, radiologists should perform a deliberate search for colocalized microhemorrhages or siderosis, as these may initially be overlooked.

Case 5: ARIA Monitoring in Comparison with CT Scan

Dr. Benzinger:

In this case, vasogenic edema in the right frontal lobe becomes more visible in the enlarged image.

Case 5: ARIA Monitoring and CT Scan

Dr. Benzinger:

The trick is that there is also a little bit of signal loss on SWI, and comparison with baseline confirms that these are not just veins in that area, but this represents new change-

Case 5: ARIA Monitoring (Grading)

Dr. Benzinger:

For classification, this is consistent with mild ARIA-E along with new susceptibility signal loss indicating additional microhemorrhages, graded as moderate ARIA-H based on lesion count. The plan would be to place a phone call to the clinical treatment team, correlate for symptoms, and recommend a follow-up scan.

Case 5: ARIA Not Seen on Head CT and CTA

Dr. Benzinger:

This is another example where a corresponding head CT failed to show the edema or hemorrhagic changes clearly. It is not well visualized, although you might think that it would be. This underscores that CT is not sensitive for typical ARIA findings and that MRI is preferred for detection and follow-up.

Case 5: Lessons Learned

Dr. Benzinger:

This was another case where a couple of the findings were missed by the original radiologist. The edema was found but not identified as ARIA. This case illustrates that radiologists may correctly recognize edema but not connect it to ARIA in the context of ATT. Education and clear communication about a patient's treatment status are essential so that radiologists can appropriately label and grade ARIA when it is present.

Case 6: Distinguishing ARIA From CAA

Dr. Benzinger:

This is a patient who came into the emergency department after a motor vehicle accident. They are visiting their family from out of town, and we do not have their medical records.

A head CT shows multifocal vasogenic edema and some focal hyperintensities concerning for hemorrhage as well.

A brain MRI including diffusion protocols shows no diffusion restriction. Diffusion is included in these protocols because the symptoms of stroke and the edema findings can overlap. There are large areas of vasogenic edema in the right temporal and right occipital lobes, and multiple microhemorrhages.

Case 6: Differential Diagnosis

Dr. Benzinger:

In the differential diagnosis, factors to consider are that the patient is being seen in the ER and we do not have a medical history. We do not know whether they are receiving ATT, but we do know that there could be trauma from the car accident. In this case, the diagnosis is CAA.

Case 6: CAA Can Resemble ARIA

Dr. Benzinger:

This case serves as a reminder that if you see something that looks like ARIA in a patient not receiving ATT, you can consider CAA as an alternative diagnosis. The vascular amyloid depositions that are responsible for a lot of the MRI features we see are a shared mechanism of CAA and ARIA.¹³

Case 7: ARIA Detection on Monitoring

Dr. Benzinger:

For the final case, we have the same 3-visit setup: baseline, monitoring, and follow-up for a patient receiving ATT.

Case 7: ARIA Detection on Monitoring (Detail)

Dr. Benzinger:

Upon inspection, vasogenic edema and sulcal effusions are noted on FLAIR, and then findings on SWI, and very subtle on the GRE/T2* as well.

Case 7: ARIA Detection on Monitoring (Grading)

Dr. Benzinger:

Findings are consistent with mild ARIA-E and moderate ARIA-H with 2 siderosis.

Case 7: Infarcts and Prior Siderosis

Dr. Benzinger:

Another important feature to highlight showed up on another MRI in the left centrum semiovale. There is a lesion with FLAIR hyperintensity but suppresses centrally, which is not the location of his ARIA. And in fact, upon inspection of his other visits, what is seen is that when he developed that FLAIR hyperintensity, it had diffusion restriction. This is an important distinction. ARIA and infarct have a lot of overlapping features on FLAIR. However, ARIA does not have diffusion restriction, and ARIA-related edema resolves over time. In this case, the patient had both processes occurring.

In the middle row, the right occipital FLAIR hyperintensity associated with the siderosis resolves on the follow-up visit. The finding in the left periventricular white matter corresponds to the infarct on a different visit. This highlights the need to watch for both of these things and distinguish ARIA from infarction; an infarct is not ARIA and requires standard stroke evaluation.

One additional finding in this case is on the very first baseline scan, there is 1 area of superficial siderosis, which is the same place where he develops ARIA later on. This reinforces the importance of carefully documenting superficial siderosis when reading that baseline MRI. In addition, when monitoring patients, areas of prior siderosis are important regions to scrutinize for subtle findings of new ARIA.

Case 7: Lessons Learned (Baseline Siderosis)

Dr. Benzinger:

This case demonstrated siderosis at baseline and then the development of ARIA-E and ARIA-H all in the same region, once again illustrating that prior siderosis is predictive of future ARIA.

Case 7: Lessons Learned (ARIA Resolution and Vascular Comorbidities)

Dr. Benzinger:

A second key lesson is that ARIA-E resolves on FLAIR, whereas an infarct does not. ARIA and ischemic infarcts can have overlapping features on FLAIR; DWI is essential to distinguish them.

Finally, AD and vascular dementia commonly coexist, and most patients have several comorbidities to consider. Radiologists should always be thinking about other pathologies that these patients can have. These are real-life patients.

AI-Assisted Neuroimaging for ARIA Detection

Dr. Benzinger:

Several artificial intelligence (AI)-assisted tools are now available to support ARIA detection and monitoring. In the US, products from Icometrix and Cortechs have received FDA clearance.^{14,15}

Potential Utility of AI-Assisted Neuroimaging

Dr. Benzinger:

These tools can assist radiologists with identifying subtle imaging features. Typically, at least 2 MRI time points are required, and automated comparison is used to identify interval changes suggestive of ARIA, such as new areas of FLAIR hyperintensity or new microhemorrhages. Many groups are using these tools and find them helpful for detecting subtle findings. The caveat is that they might also introduce additional false positives or quality control questions that require follow-up.¹⁶⁻¹⁸ These tools certainly cannot replace radiologists, but can definitely be included in workflows for many radiology groups. Although AI tools can help with standardization and inter-reader variability, independent review and final interpretation by a radiologist is essential.

Conclusion and Future Directions

Dr. Benzinger:

It is very exciting to finally be at a time we have long waited for, with disease-modifying treatment available to patients with AD, and amazing that radiology is so central to this patient care. It is truly an honor and a privilege to be able to participate in these patient journeys.

Dr. Lövblad:

I agree, it is an exciting revolution, first for the patients, but also for us as radiologists. It means that we will have a new flow of patients to manage, which is a challenge in terms of resources. Here in Switzerland, we triage the population a bit as compared to the US in order to concentrate the patients around memory clinics, at least at the beginning of treatment. In Switzerland, as in the US, we do have lots of scanners, but we might still need to extend operating hours or make other adjustments to accommodate these new patients.

Dr. Benzinger:

Building protocols early, with dedicated studies on the scanner, helps to allow short, focused exams. For us, 100 patients on ATT meant 1000 new brain MRIs to perform, and as the patient number increases, the number of MRIs keeps scaling. Every patient that begins therapy needs 6 MRIs, and for every 1 of those patients, 3 or 4 more had baseline MRIs but failed screening. In total, it is an enormous practice implementation.

Dr. Lövblad:

The numbers will likely continue to grow, taking into account the increasing age of the population and improved methods for detection and screening. This represents a significant milestone for the whole radiology community and an immense opportunity to help support patients and referring HCPs.

Guidelines and Resources for Dementia Imaging

Multiple professional organizations have developed comprehensive guidelines and resources relevant to dementia imaging and ARIA monitoring. These include:

- Alzheimer's Association/Society for Nuclear Medicine and Molecular Imaging Appropriate Use for Amyloid and Tau PET, 2025

[Link to: <https://acsearch.acr.org/docs/3111292/Narrative>]

- American Society for Neuroradiology Recommendations, 2022 & 2025. [Link to: <https://www.ajnr.org/content/43/9/E19.abstract> and <https://www.ajnr.org/content/46/1/24.abstract>]
- European Consensus for the Diagnosis of MCI and Early AD, European Society of Neuroradiology and the European Association of Nuclear Medicine (EANM), 2023. [Link to: <https://pubmed.ncbi.nlm.nih.gov/36209379/>]
- American College of Radiology Appropriateness Criteria for Dementia Imaging, 2024. [Link to: [https://www.jacr.org/article/S1546-1440\(25\)00137-1/fulltext](https://www.jacr.org/article/S1546-1440(25)00137-1/fulltext)]
- Treatment-related amyloid clearance, Alzheimer's & Dementia, 2025. [Link to: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12657122/>]
- Swiss Society for Neuroradiology, 2025 [Link to: <https://karger.com/ndd/article/doi/10.1159/000549521/939032/Clinical-practice-recommendations-of-the-Swiss>]

These resources provide practical protocols, example reporting templates, and workflows that radiology practices can adopt or adapt to their local environment. Reviewing these resources can help teams build robust, scalable approaches to ARIA monitoring and dementia imaging more broadly.