



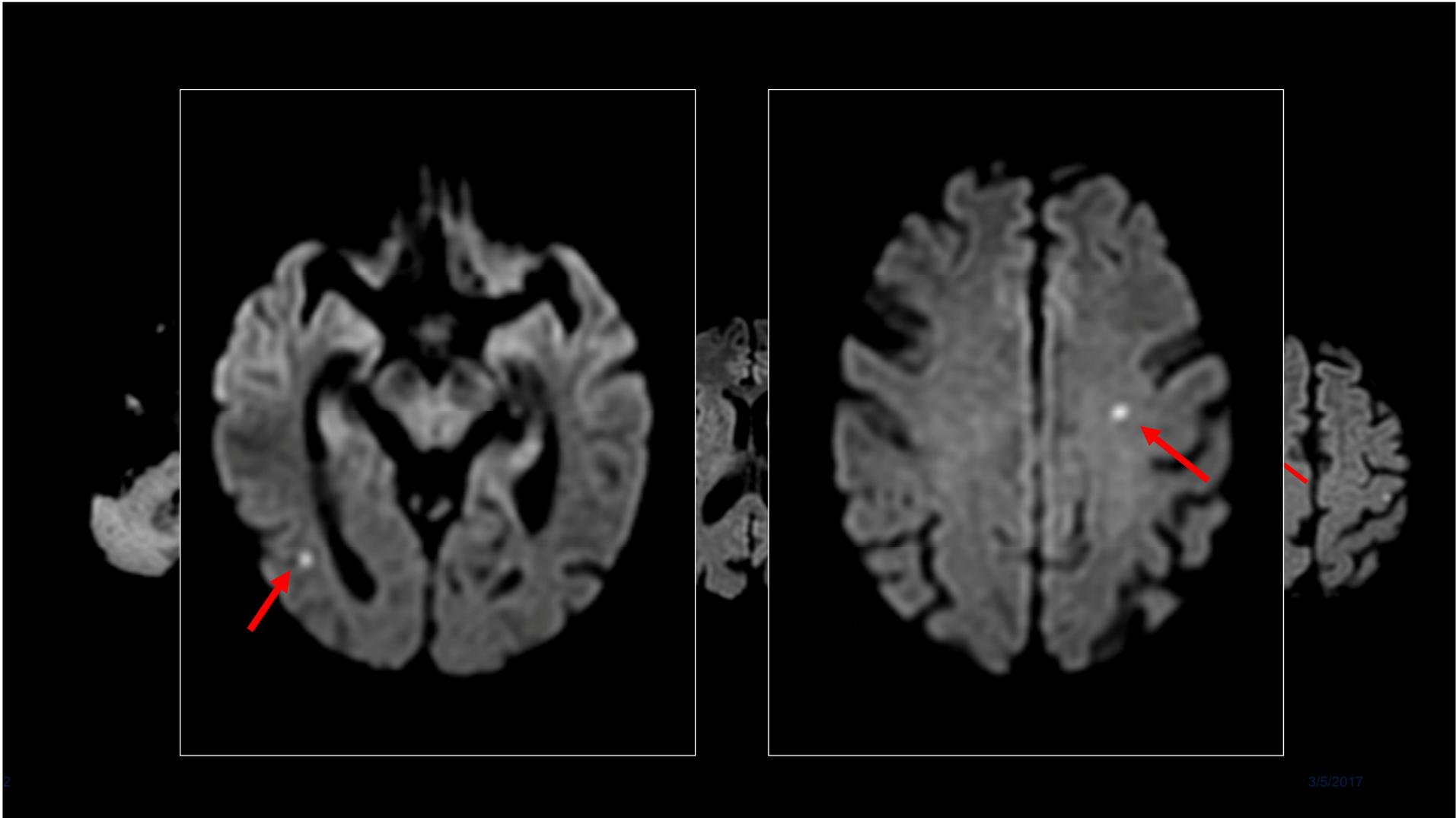
University of California
San Francisco

Post TAVR Abnormalities by DWI MR

What do they mean?

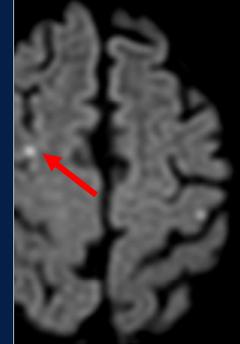
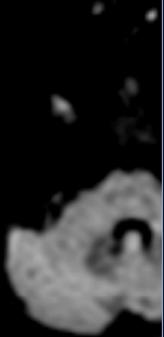
Christopher P. Hess, MD, PhD
Professor and Chief, UCSF Neuroradiology

3/5/2017



MESSAGE

DWI lesions post TAVR represent the earliest detectable imaging finding of irreversible brain cell death. Even when **clinically silent**, these reflect small infarcts.



ORGANIZATION

1. **Observations:** What do we see with DWI after TAVR?
2. **Physics:** What is being measured with DWI?
3. **Pathology:** Why do we see DWI lesions in ischemic injury?

1. Observations: *Background – DWI & TAVR*

- Common! 58-100% of cases after TAVR
- Incidence not significantly reduced by bivalirudin (BRAVO-3)¹
- Increased with longer catheter and fluoro times², aortic atheroma³, guidewire manipulation (especially through stenotic valve⁴)
- Probably reduced by EPD's⁵⁻⁷
- Clinically silent in majority of patients

1. Van Belle et al, JACC 2016
2. Busing et al, Radiology 2005
3. Fairbain et al, Heart 2012
4. Omran et al, Lancet 2003
5. Haussig et al, JAMA 2016
6. Lansky et al, Eur J Heart 2016
7. Kapadia et al, JACC 2017

1. Observations: *Common features of DWI lesions*

- Small size, peripheral location → **end-vessel**
- Reduced diffusion → **ischemic**
- Scattered in multiple vascular territories → **embolic**
- Non-hemorrhagic
- **NeuroARC¹ 2.a** lesions

THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

Proposed Standardized Neurological Endpoints for Cardiovascular Clinical Trials



An Academic Research Consortium Initiative

TABLE 4 MRI Endpoint Reporting Recommendations

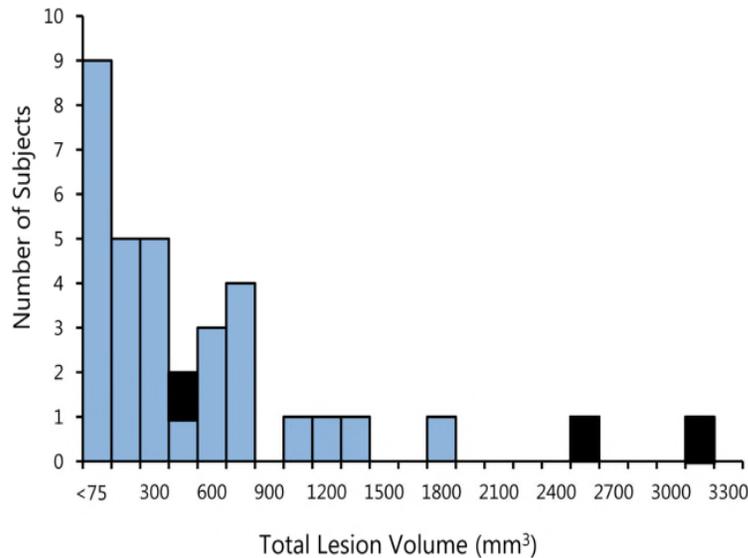
Primary Endpoint	Total Lesion Volume (mm ³) (Median, IQR, Min and Max)
Other endpoints	<ul style="list-style-type: none">• Incidence (%): Proportion of patients with new post-procedure DWI lesions• Number of lesions• Single lesion volume (mm³): (median, IQR)• Maximum lesion volume (mm³): (median, IQR)
Analysis considerations	<ul style="list-style-type: none">• Endpoints should be reported for the overall population, the population of patients with overt CNS injury, and those with covert CNS injury

DWI = diffusion-weighted imaging; IQR = interquartile range; other abbreviations as in Tables 1 and 2.

1. Lansky et al, JACC 2017

1. Observations: *Common features of DWI lesions*

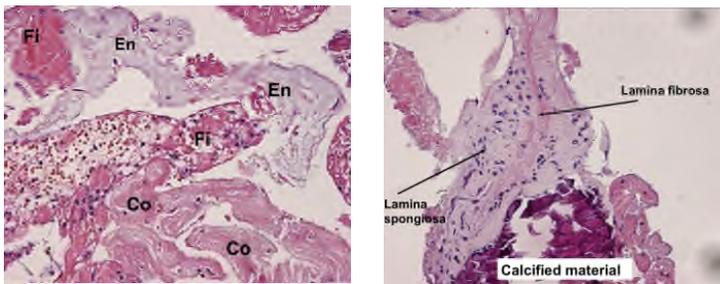
Neuro-TAVI¹



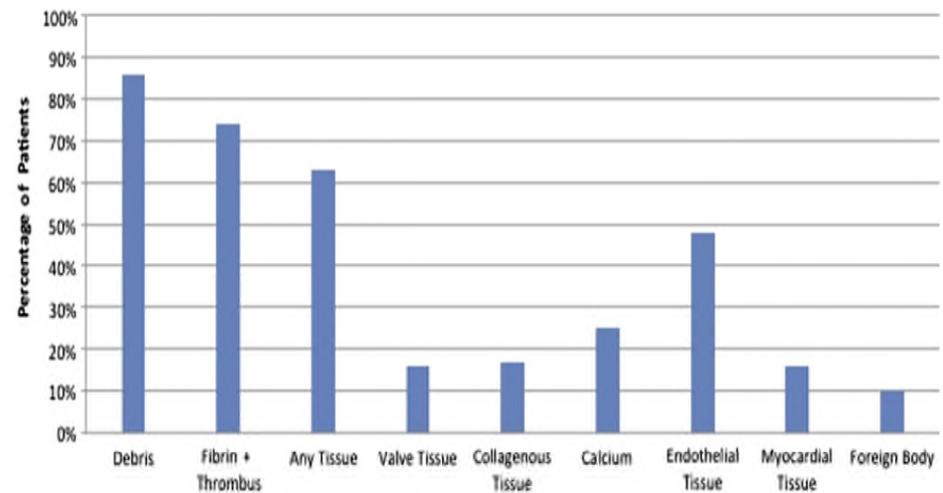
- DWI lesions in 94%
- MRI @ 4 days
- Mean 10.4 lesions per subject
- Median single DWI volume 49 mm³
- Median total DWI volume 295 mm³
- Larger → more likely symptomatic

1. Lansky et al, Am J Cardiol 2016

1. Observations: *What do we see with DWI after TAVR ?*



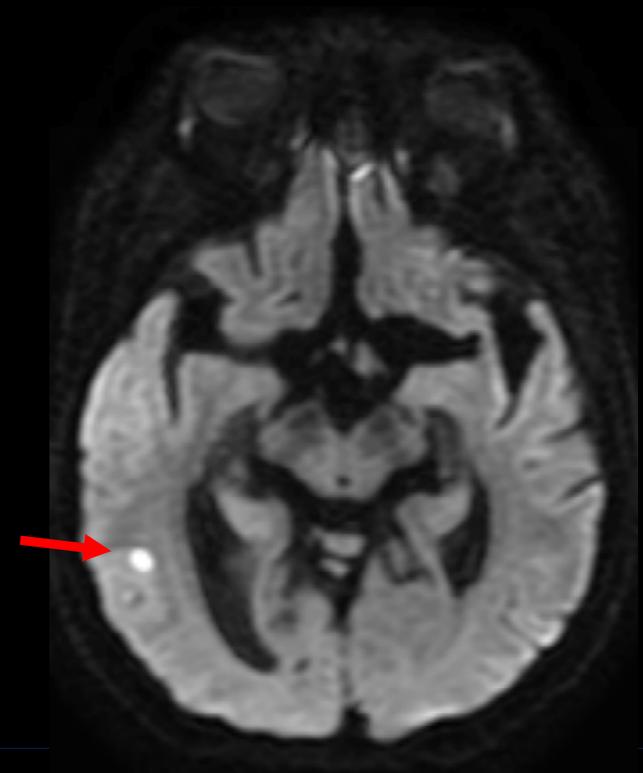
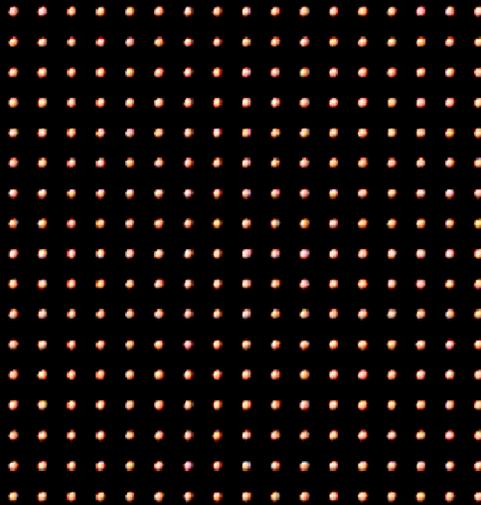
- Median particle **1 mm (0.1-9mm)**
- Fibrin & thrombus in **74%**
- Tissue-derived debris in **63%**
- Fragments of valve in **33%**



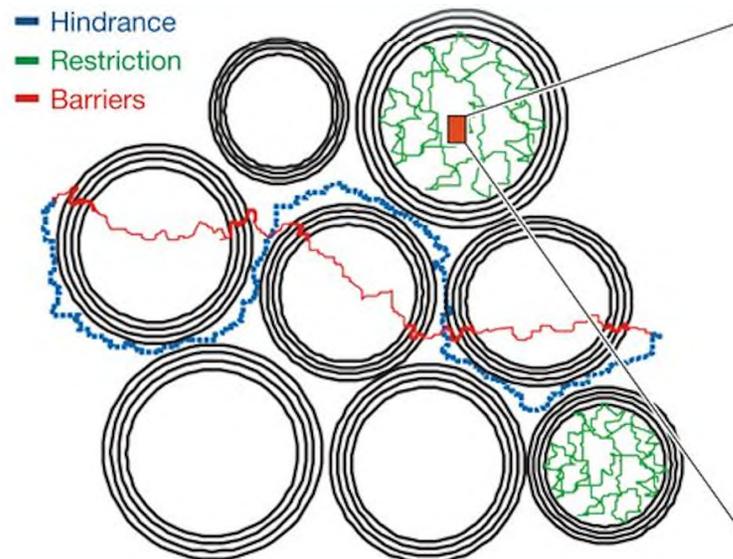
Van Mieghem et al, JACC Cardiovasc Int 2015

2. Physics: *What is being measured with DWI?*

- Net random displacement of water molecules over a measurement time
- Displacement \rightarrow image intensity
- Dark = fast, bright = slow
- Dependent upon location at the micron scale
- 3T more sensitive than 1.5T
 \uparrow signal, \uparrow resolution



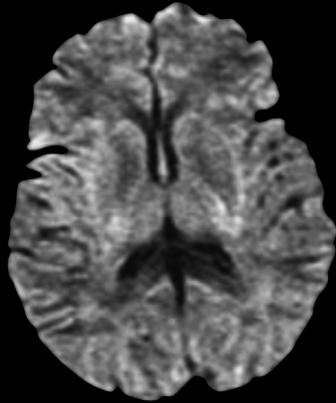
2. Physics: *What is being measured with DWI?*



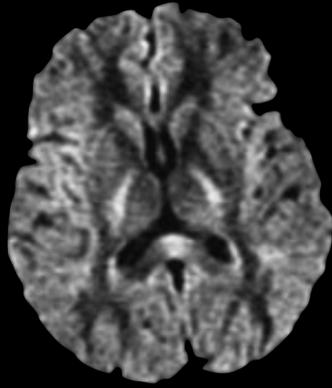
- Axonal membranes
- Myelin
 - Neurofilaments
 - Microtubules
 - Macromolecules
 - Organelles
- ... anything other than water!

2. Physics: *What is being measured with DWI?*

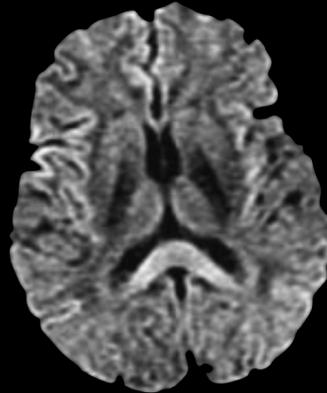
- White matter bundles → directional anisotropy
- Combine to remove anisotropy effects
- DWI is pixel-wise map of how fast water is moving



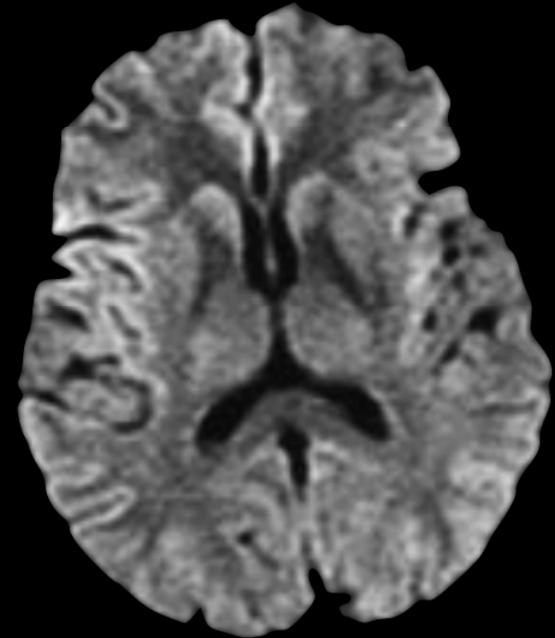
G_x



G_y



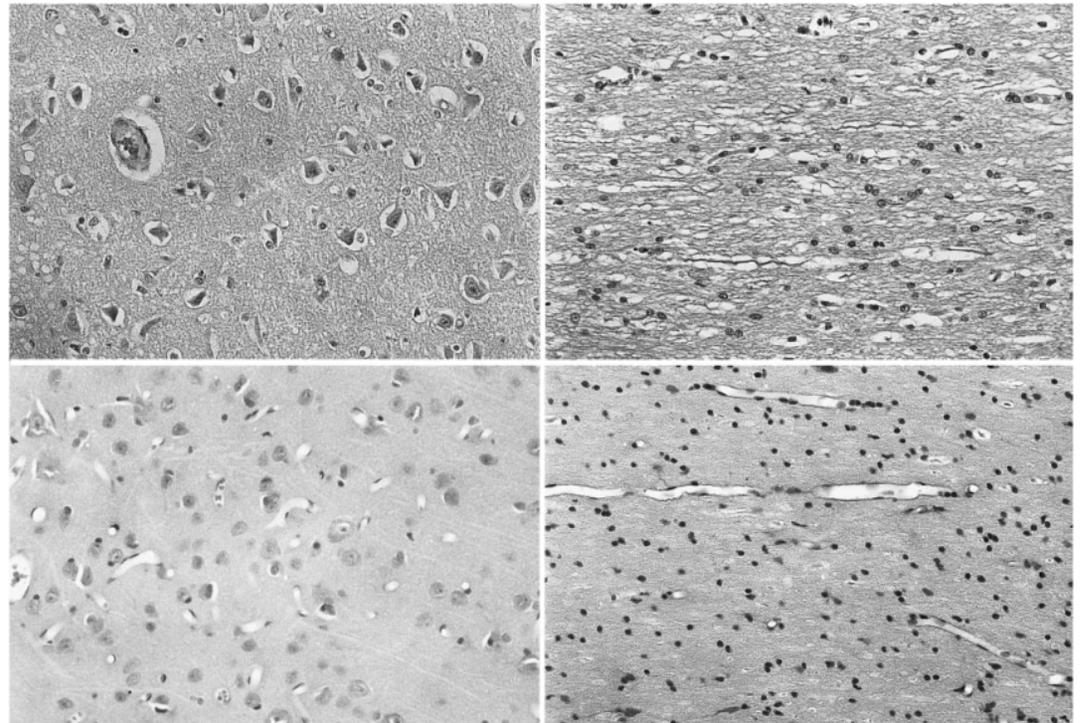
G_z



“Average Image” = DWI

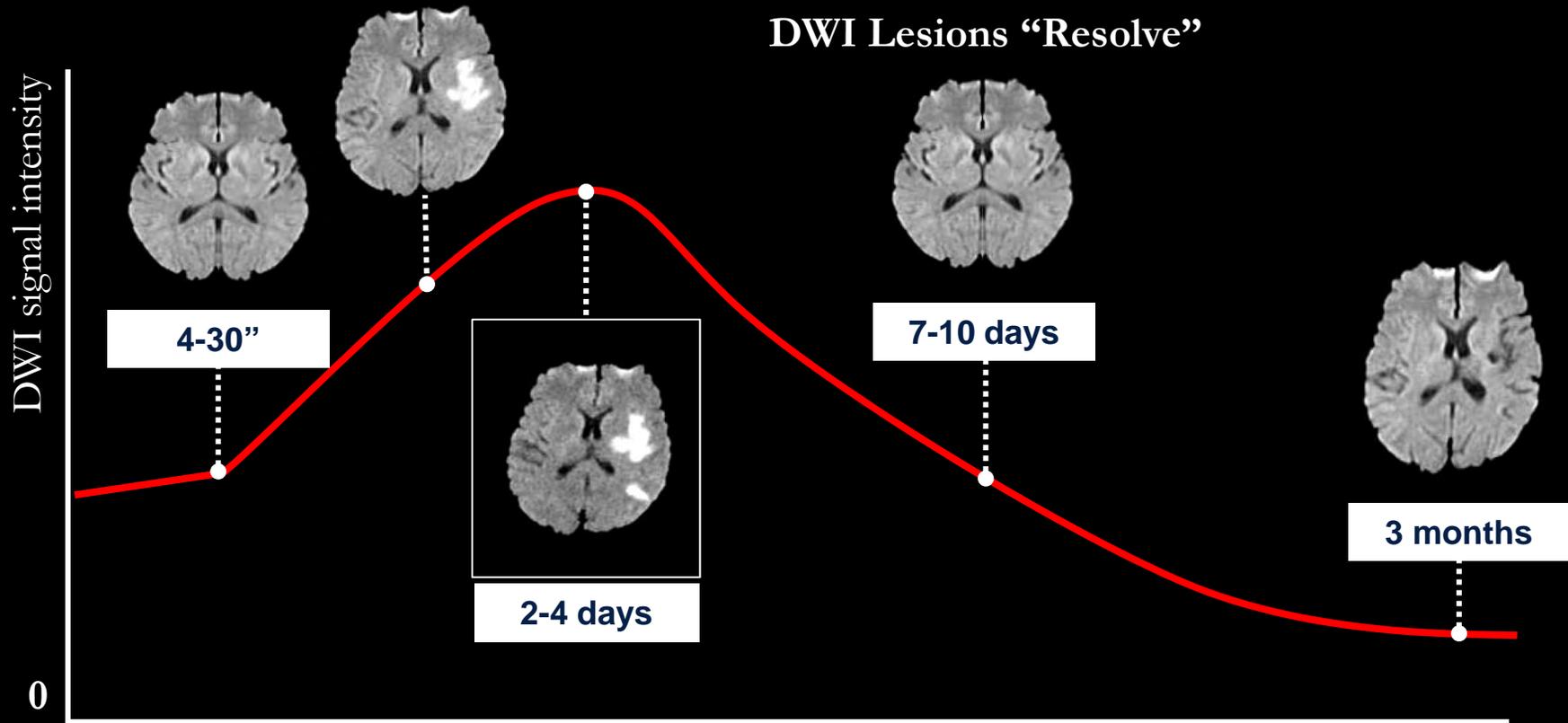
3. Pathology: *Why is DWI reduced in ischemic tissue?*

- Na⁺/K⁺ pump failure causes net intracellular shift in water
- Cellular swelling
- Neuritic beading limits normal diffusion of intracellular and extracellular water diffusion
- Rate of diffusion decreases
- Hydropic neurons = cytotoxic edema, which is **irreversible**



Kuroiwa et al, Stroke 1998

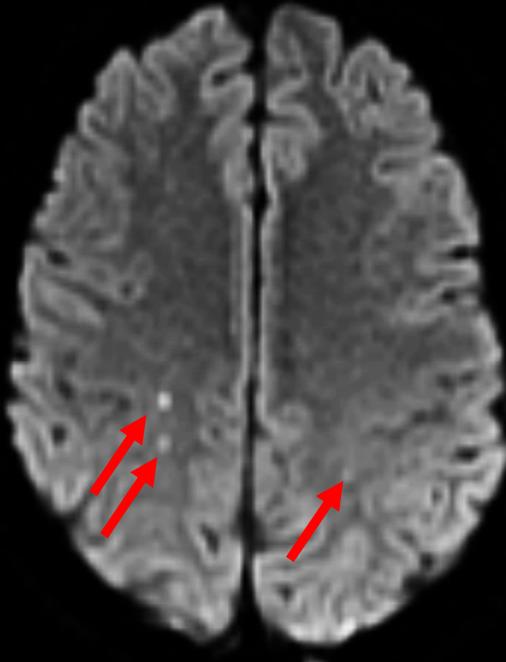
3. Pathology: *Caveats to linking DWI and pathology*



3. Pathology: *The natural evolution of ischemic on DWI*

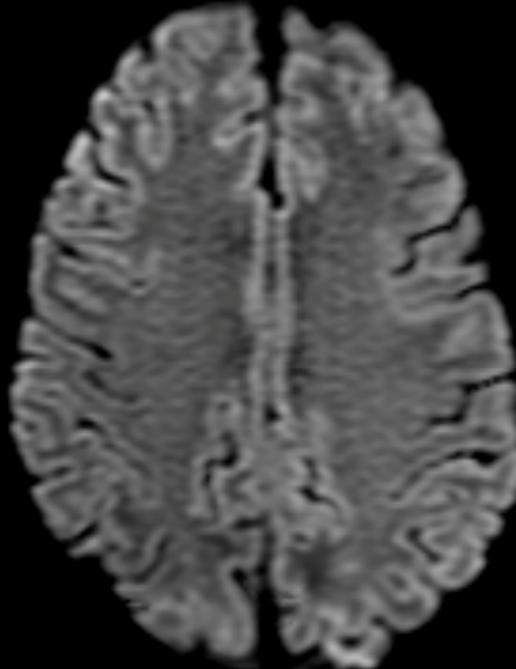
DWI

2 days post procedure



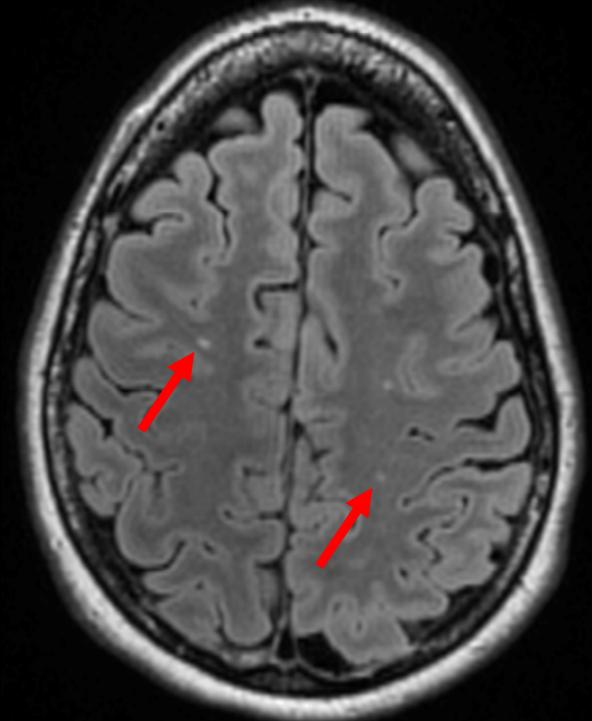
DWI

17 days post procedure



T2 FLAIR

17 days post procedure



Summary: *What do DWI lesions mean after TAVR?*

- Clinical strokes are uncommon after TAVR, but DWI lesions are common
- Lesions reflect tiny infarcts from end-artery occlusions due to embolic debris
- Reduced diffusion on imaging = cytotoxic edema pathologically = cell death
- The conspicuity of lesions depends upon biological and technical parameters
 - Timing of MRI after procedure
 - Field strength and gradient performance of MRI scanner
 - DWI technique: slice thickness, in-plane spatial resolution, acceleration
- DWI lesions naturally evolve into T2 lesions, probably tip of the iceberg



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