

Retrospektiv analyse av glioblastom

Ideer for andre publikasjon

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onsdag 8. september 2021

Disposisjon

1. Longitudinell data - SAILOR, etc.
2. Prediksjon av RANO (1-4) og pseudoprogresjon (5?)
3. Prediksjon av neste bilde basert på forflytning og intensitetsendring
4. Eksplorativ analyse av behandlingsforløp

1. Longitudinell data

1



178

255

SAILOR, T1c, pas. 1

Level

Window

2



SAILOR, T1c, pas. 1



3



SAILOR, T1c, pas. 1



4



SAILOR, T1c, pas. 1



5



SAILOR, T1c, pas. 1

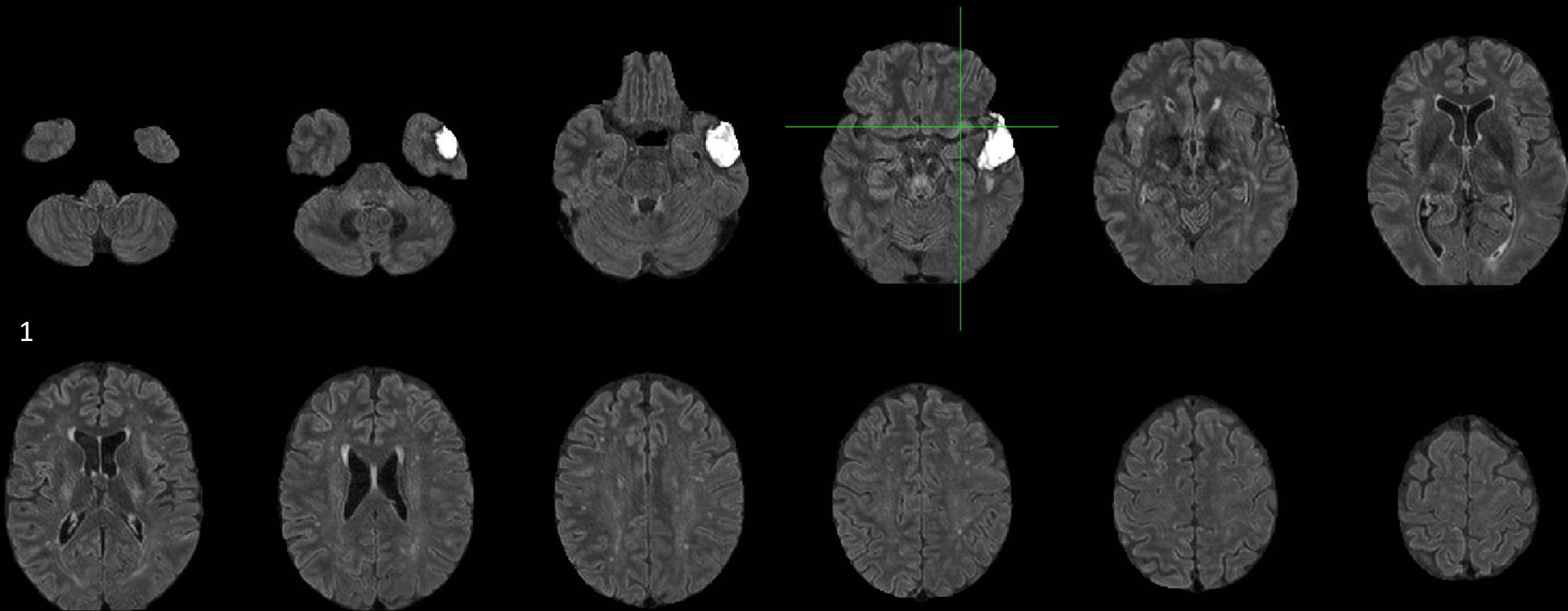


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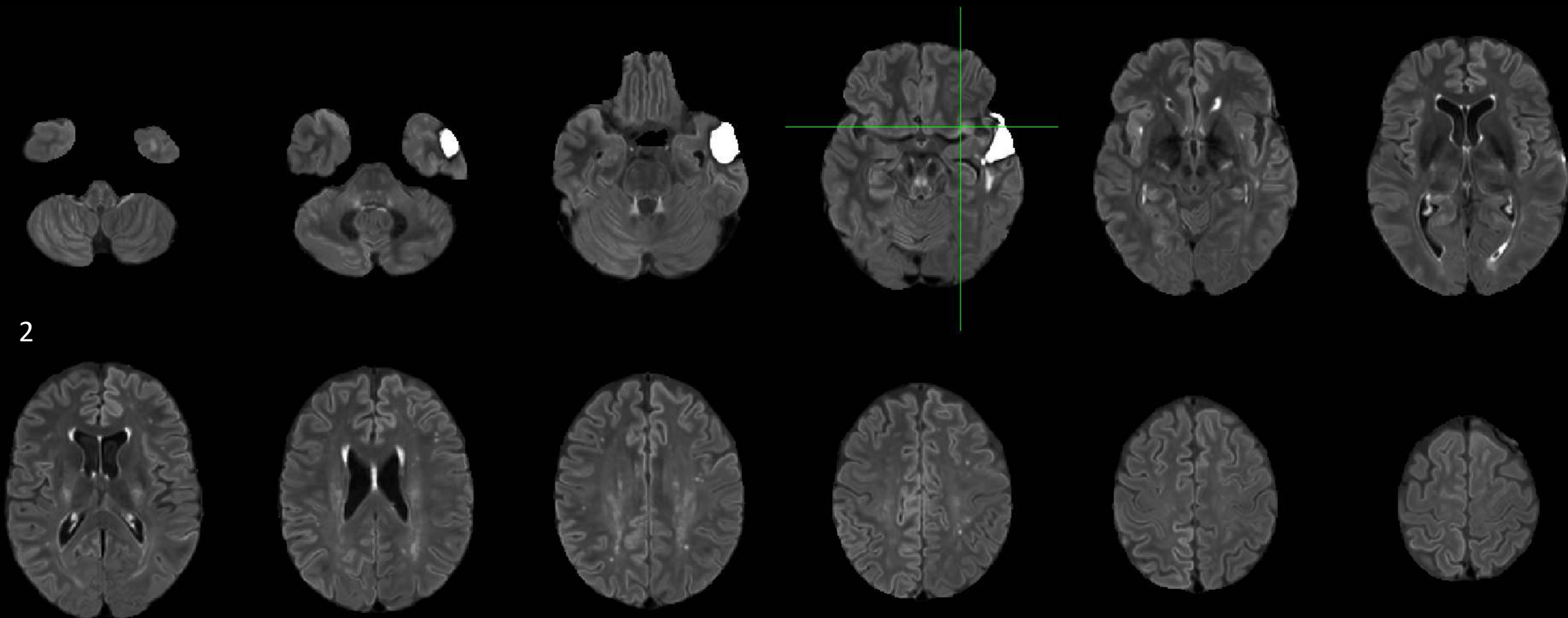
SAILOR, T1c, pas. 1





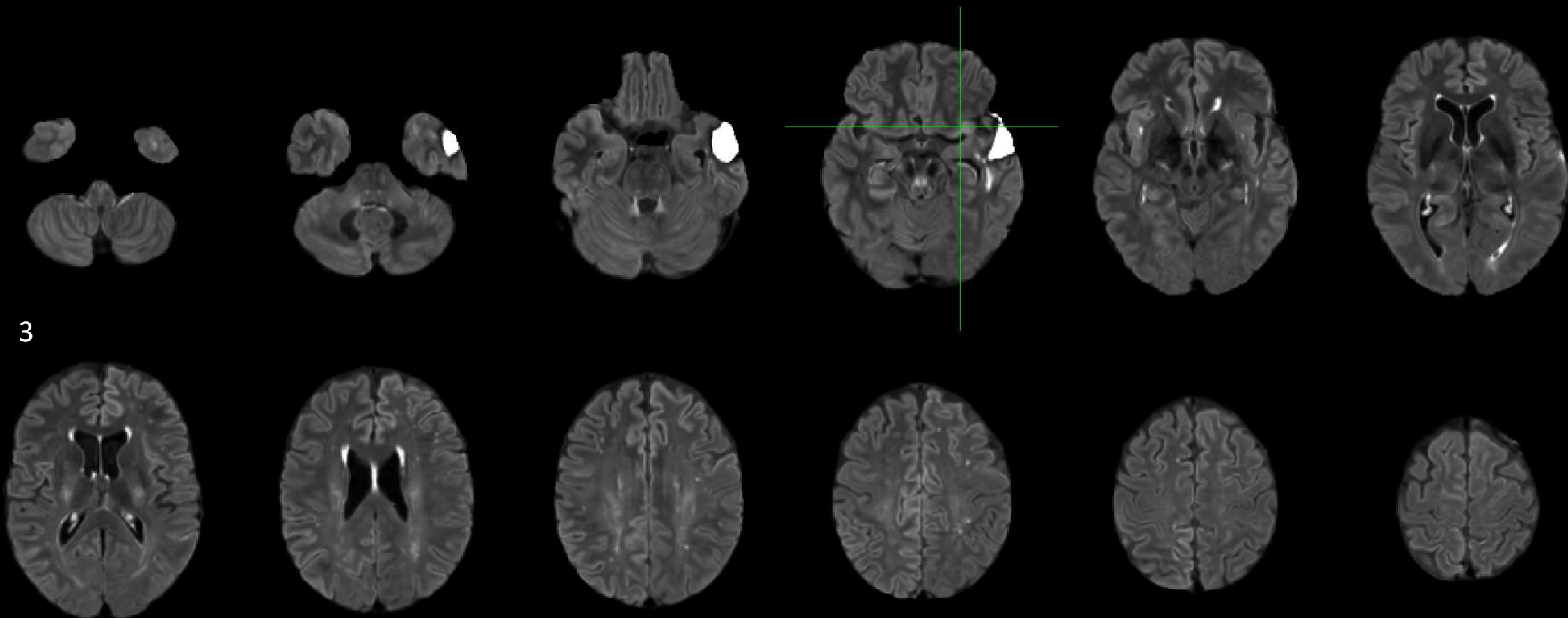
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SAILOR, FLAIR, pas. 4



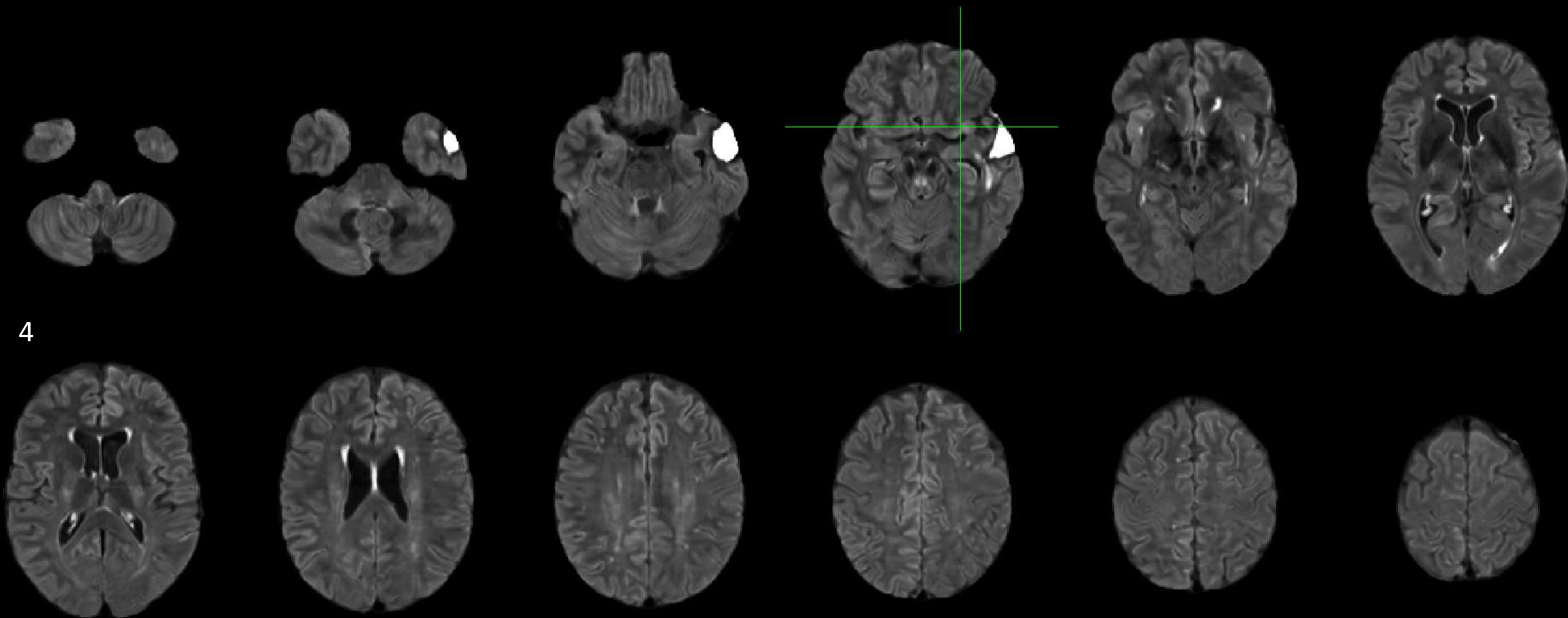
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SAILOR, FLAIR, pas. 4



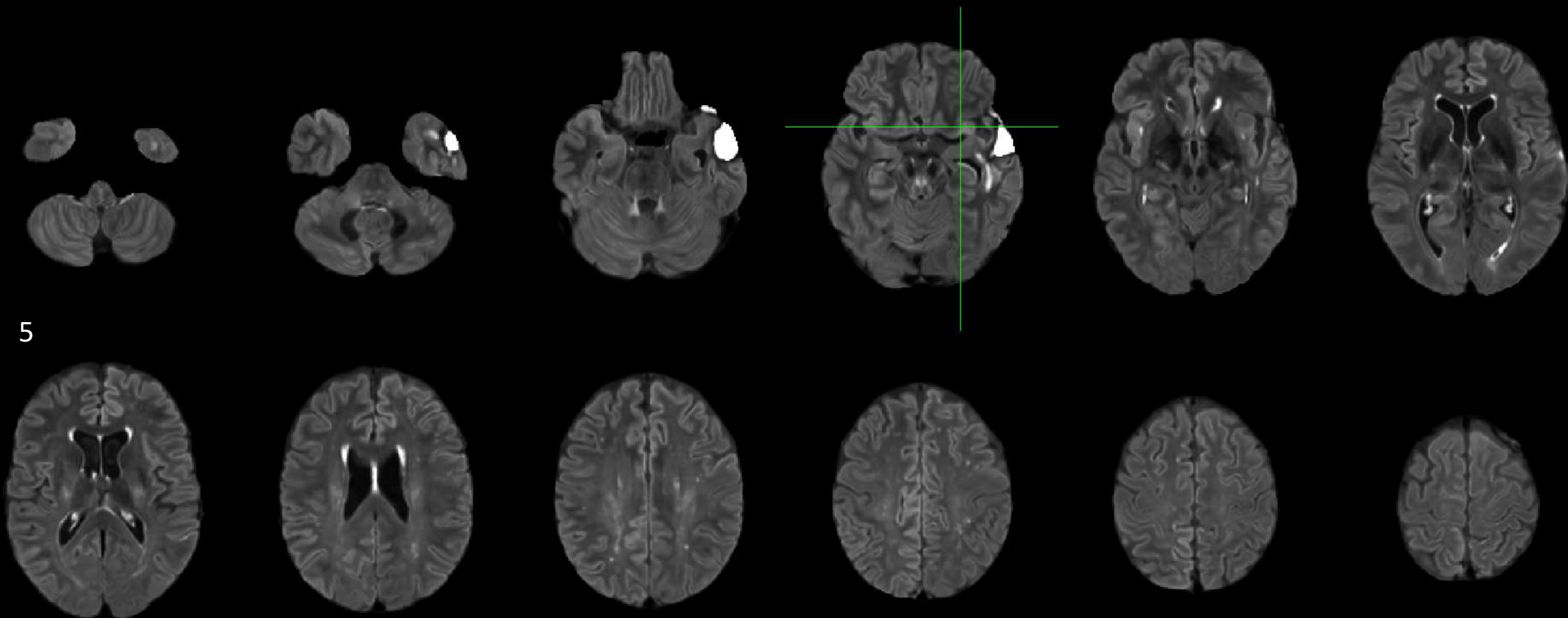
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SAILOR, FLAIR, pas. 4

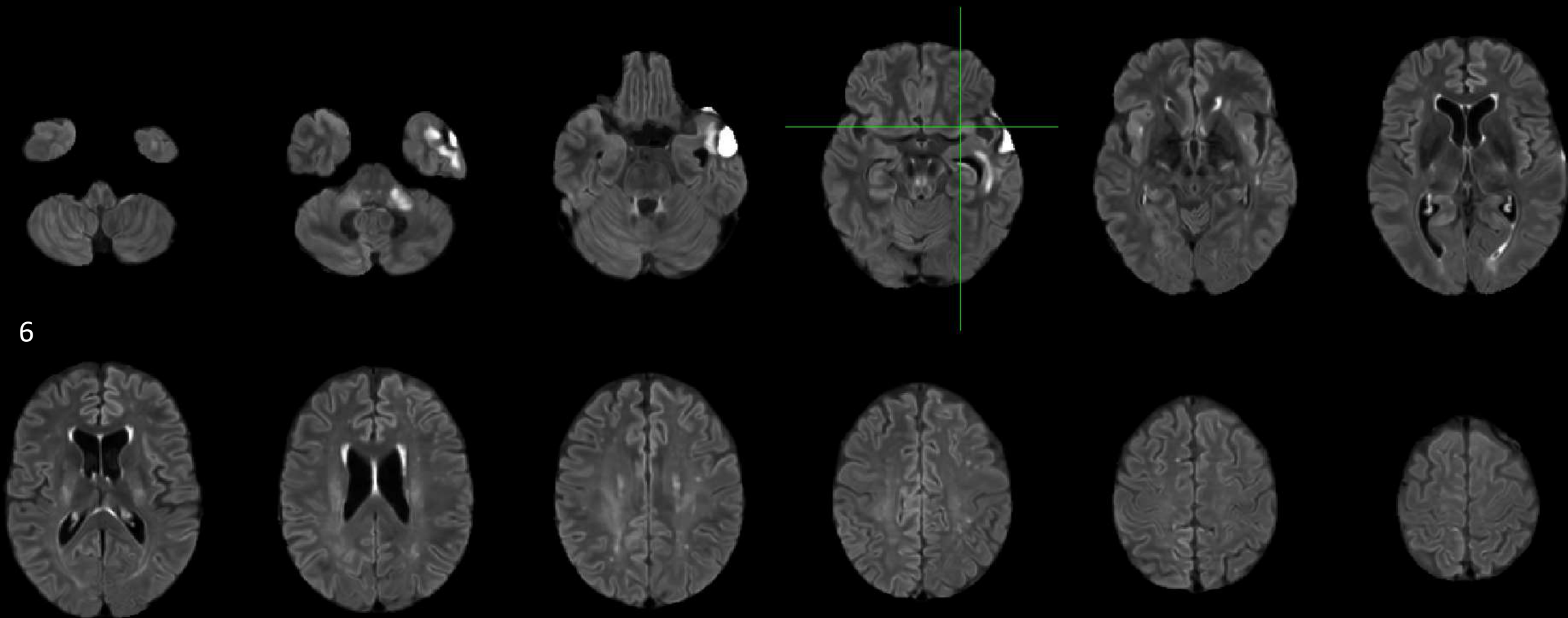


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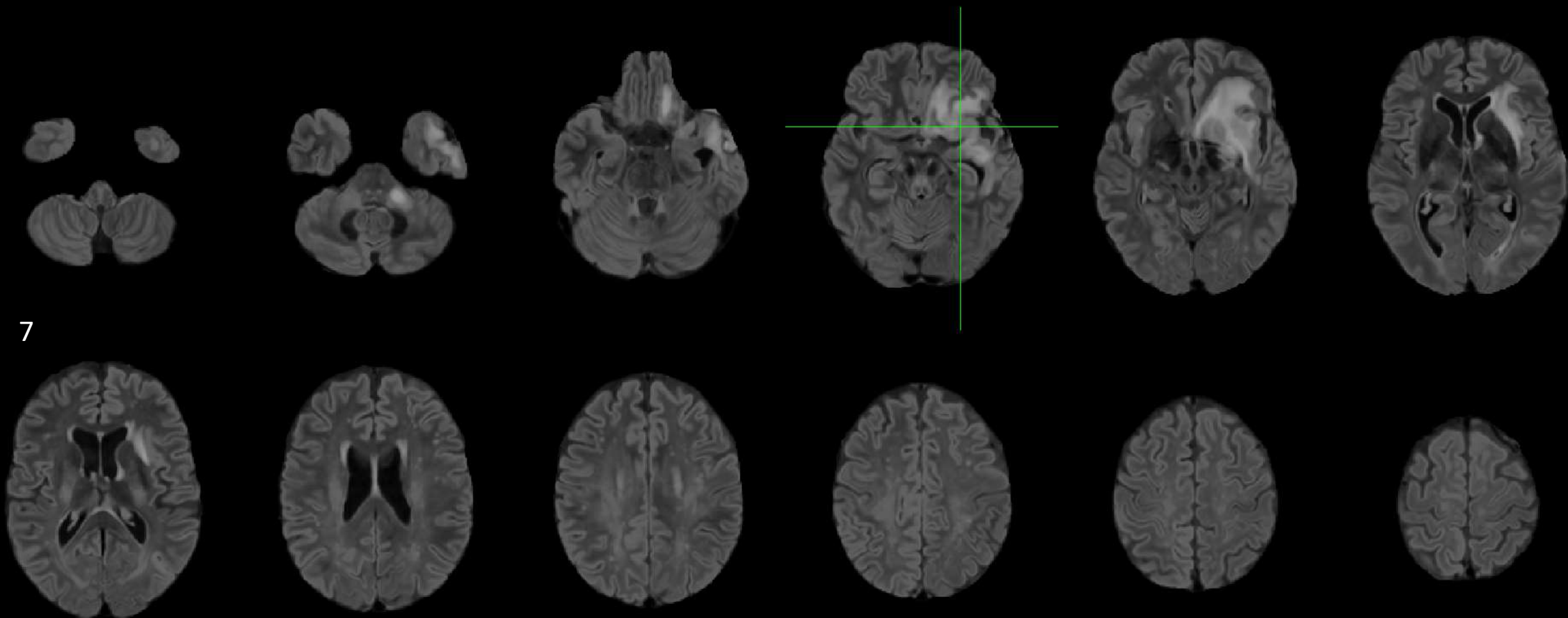
SAILOR, FLAIR, pas. 4



SAILOR, FLAIR, pas. 4

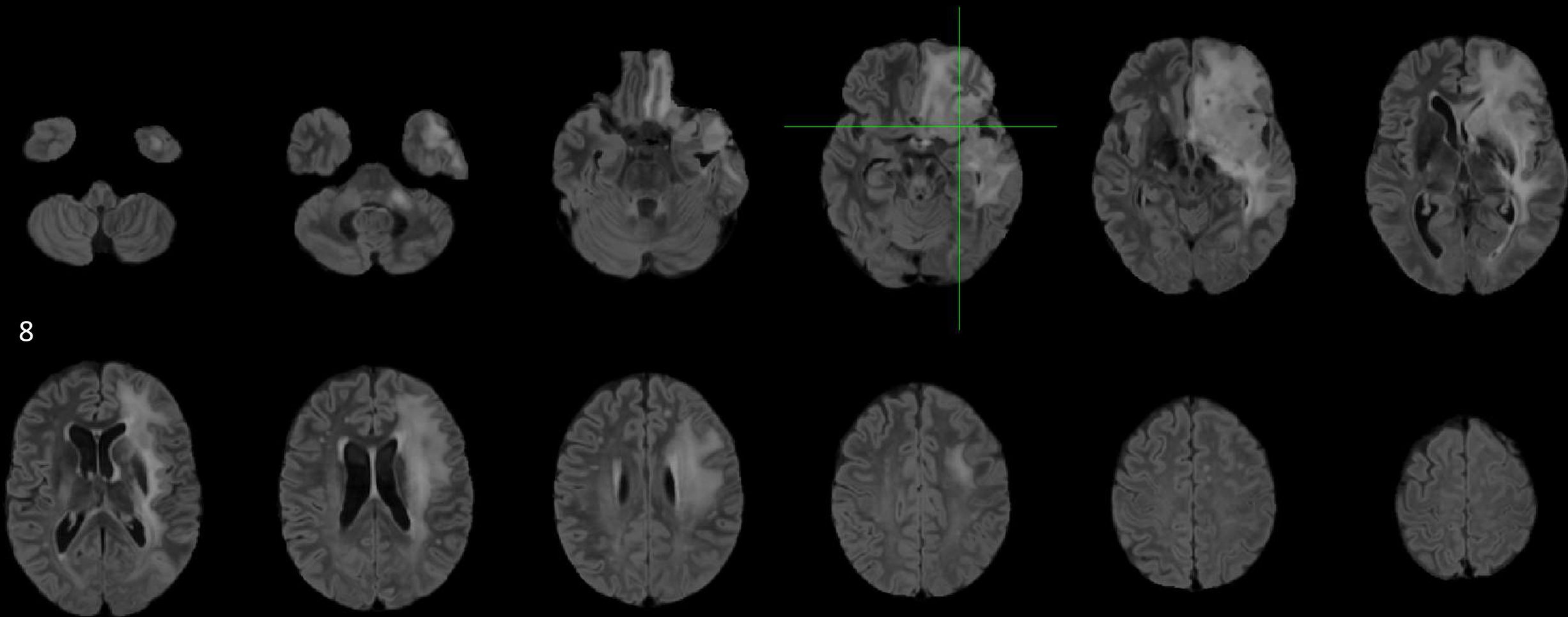


SAILOR, FLAIR, pas. 4



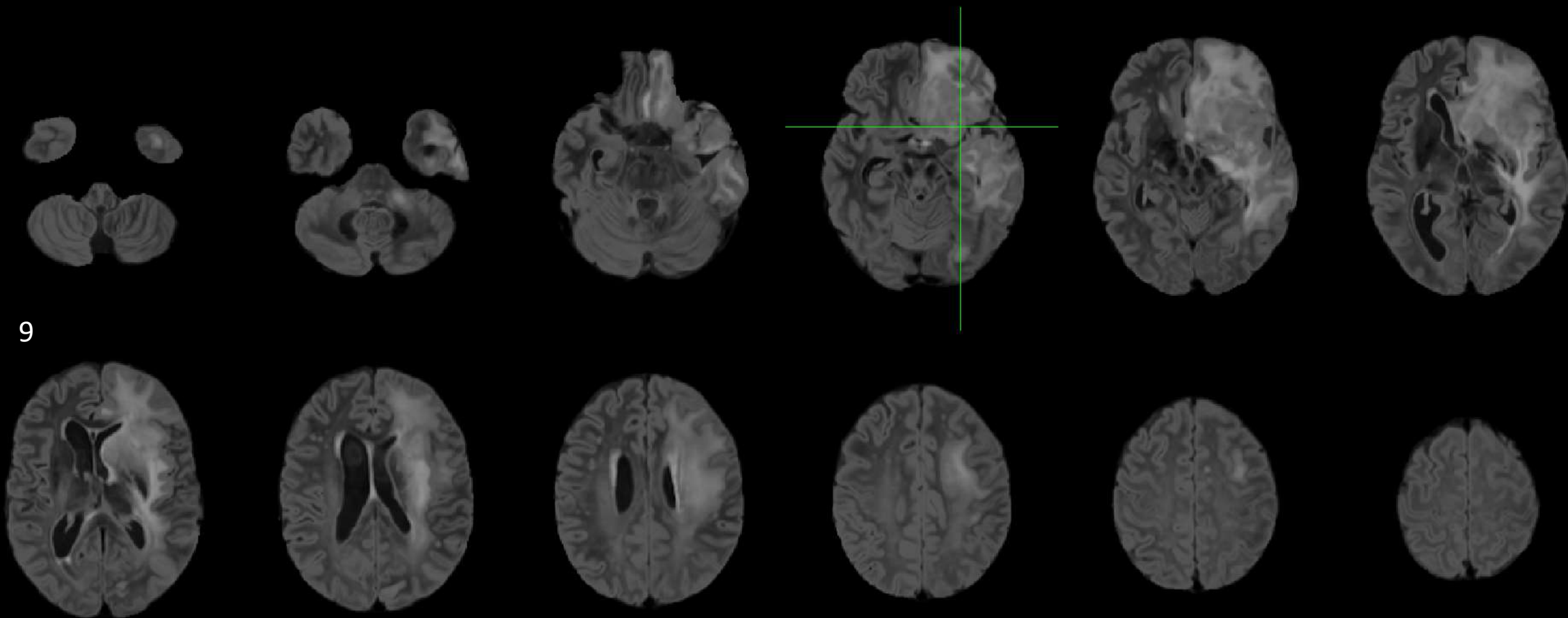
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SAILOR, FLAIR, pas. 4



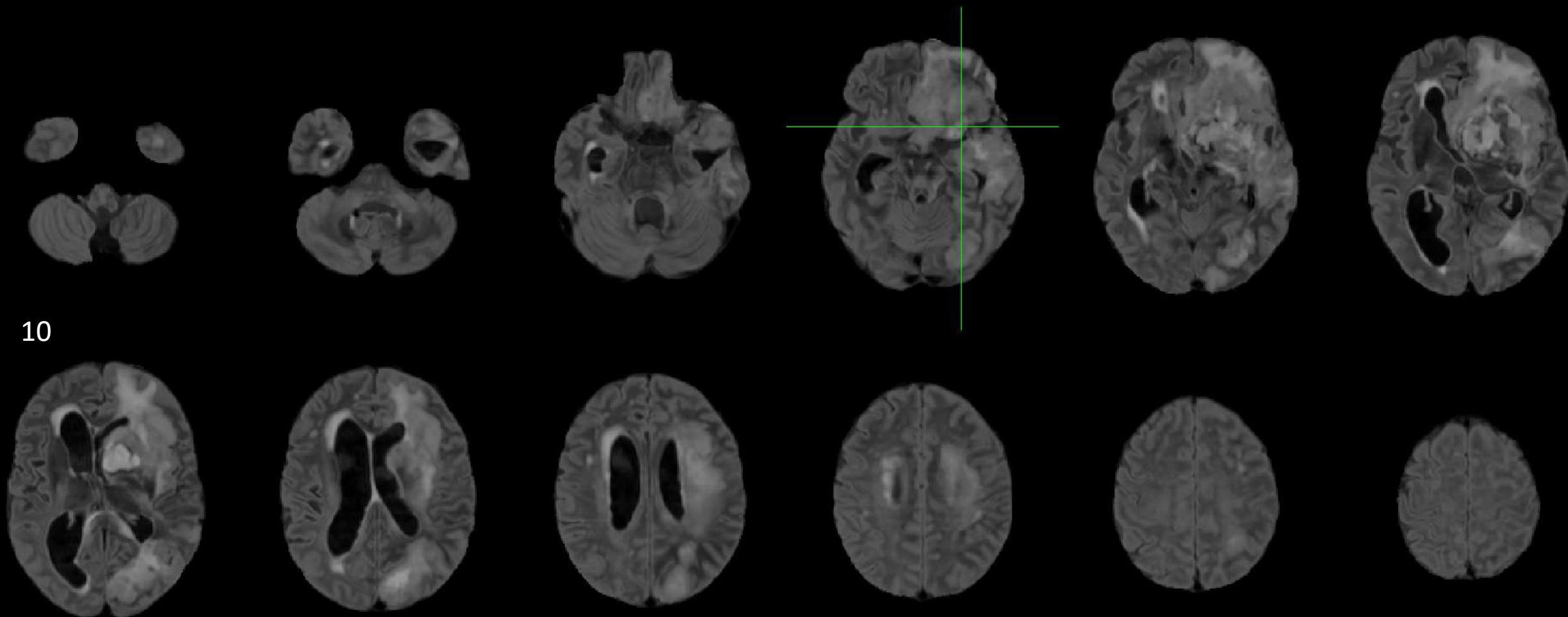
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SAILOR, FLAIR, pas. 4



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SAILOR, FLAIR, pas. 4



10

SAILOR, FLAIR, pas. 4

Heterogenitet

1. Response Assessment in Neuro-Oncology (RANO)

- Klassifisering av behandlingsrespons basert på to tidspunkter
- Basert på (endring av) to lengste vinkelrette diametermål av tumor, T2/FLAIR-endringer og annen informasjon
- Complete response, partial response, stable disease, progression

2. Ulik grad av suksess fra behandling (forrige slides)

- Opprinnelig tumor krymper fra behandling, vokser så igjen i samme område, eller nye tumorer oppstår
- Kan føre til deformasjon og/eller intensitetsendringer i bilde
- Bildeendringer en kombinasjon av respons fra behandling og kreft

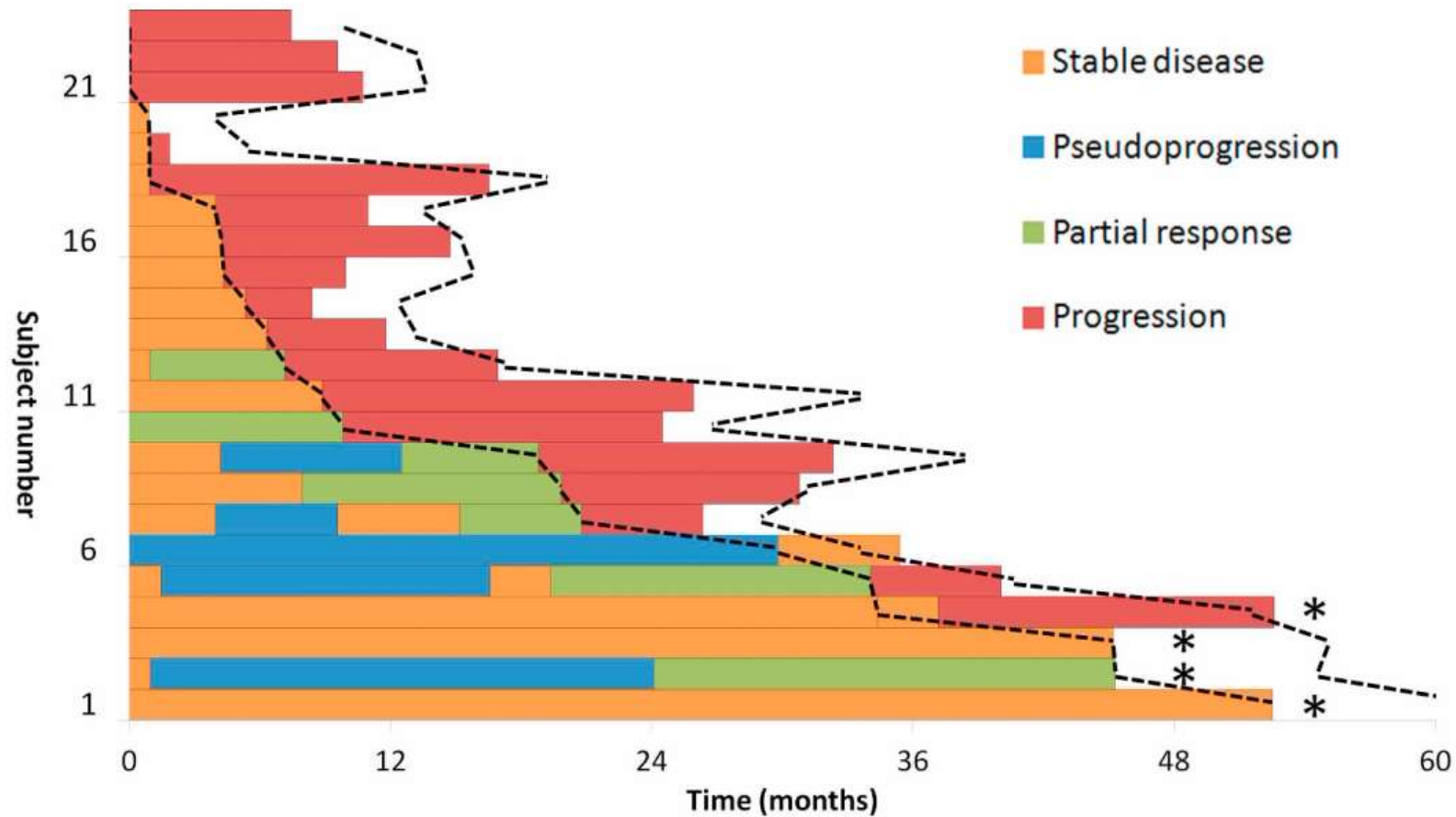
Heterogenitet – RANO

Wen, Patrick Y., et al. "Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group." *Journal of clinical oncology* 28.11 (2010): 1963-1972.

Table 3. Criteria for Response Assessment Incorporating MRI and Clinical Factors

Response	Criteria
Complete response	Requires all of the following: complete disappearance of all enhancing measurable and nonmeasurable disease sustained for at least 4 weeks; no new lesions; stable or improved nonenhancing (T2/FLAIR) lesions; patients must be off corticosteroids (or on physiologic replacement doses only); and stable or improved clinically. Note: Patients with nonmeasurable disease only cannot have a complete response; the best response possible is stable disease.
Partial response	Requires all of the following: $\geq 50\%$ decrease compared with baseline in the sum of products of perpendicular diameters of all measurable enhancing lesions sustained for at least 4 weeks; no progression of nonmeasurable disease; no new lesions; stable or improved nonenhancing (T2/FLAIR) lesions on same or lower dose of corticosteroids compared with baseline scan; the corticosteroid dose at the time of the scan evaluation should be no greater than the dose at time of baseline scan; and stable or improved clinically. Note: Patients with nonmeasurable disease only cannot have a partial response; the best response possible is stable disease.
Stable disease	Requires all of the following: does not qualify for complete response, partial response, or progression; stable nonenhancing (T2/FLAIR) lesions on same or lower dose of corticosteroids compared with baseline scan. In the event that the corticosteroid dose was increased for new symptoms and signs without confirmation of disease progression on neuroimaging, and subsequent follow-up imaging shows that this increase in corticosteroids was required because of disease progression, the last scan considered to show stable disease will be the scan obtained when the corticosteroid dose was equivalent to the baseline dose.
Progression	Defined by any of the following: $\geq 25\%$ increase in sum of the products of perpendicular diameters of enhancing lesions compared with the smallest tumor measurement obtained either at baseline (if no decrease) or best response, on stable or increasing doses of corticosteroids; significant increase in T2/FLAIR nonenhancing lesion on stable or increasing doses of corticosteroids compared with baseline scan or best response.

Heterogenitet – RANO i SALOR



Wen, Patrick Y., et al. "Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group." Journal of clinical oncology 28.11 (2010): 1963-1972.

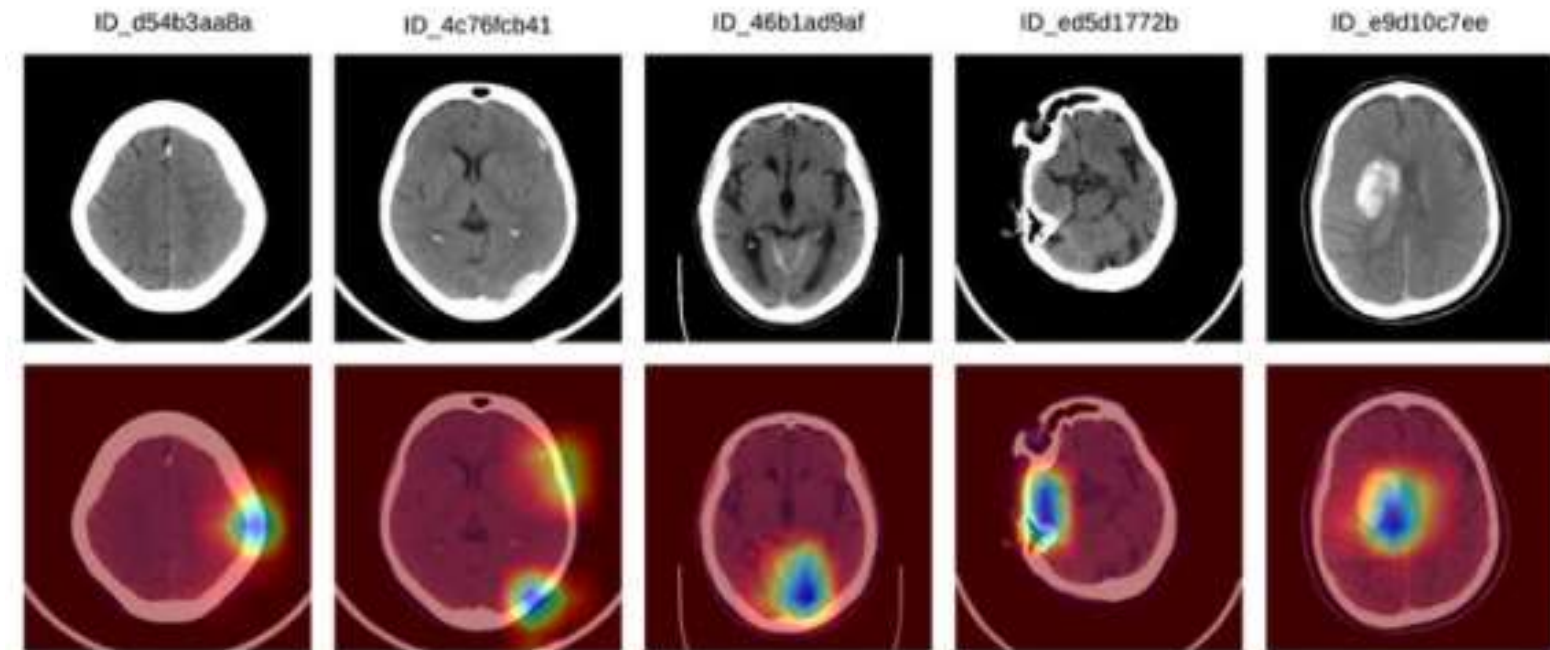
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- Fordeler:
 - Basert på bilder fra ett tidspunkt, prediker RANO-klasse som ville blitt gitt basert på dette og neste tidspunkt
 - Egnet løst av dyp læring enkoder-struktur, rett frem å implementere (allerede implementert)
 - Kan bruke forklarbare metoder (explainable AI) for tolkning av DL-modell
- Ulemper:
 - Ubalansert fordeling av RANO-klasser i SAILOR
 - Behov for flere pasienter og oppfølginger med RANO fra andre datasett

GRAD-CAM eksempel

(Gradient-weighted Class Activation Mapping)

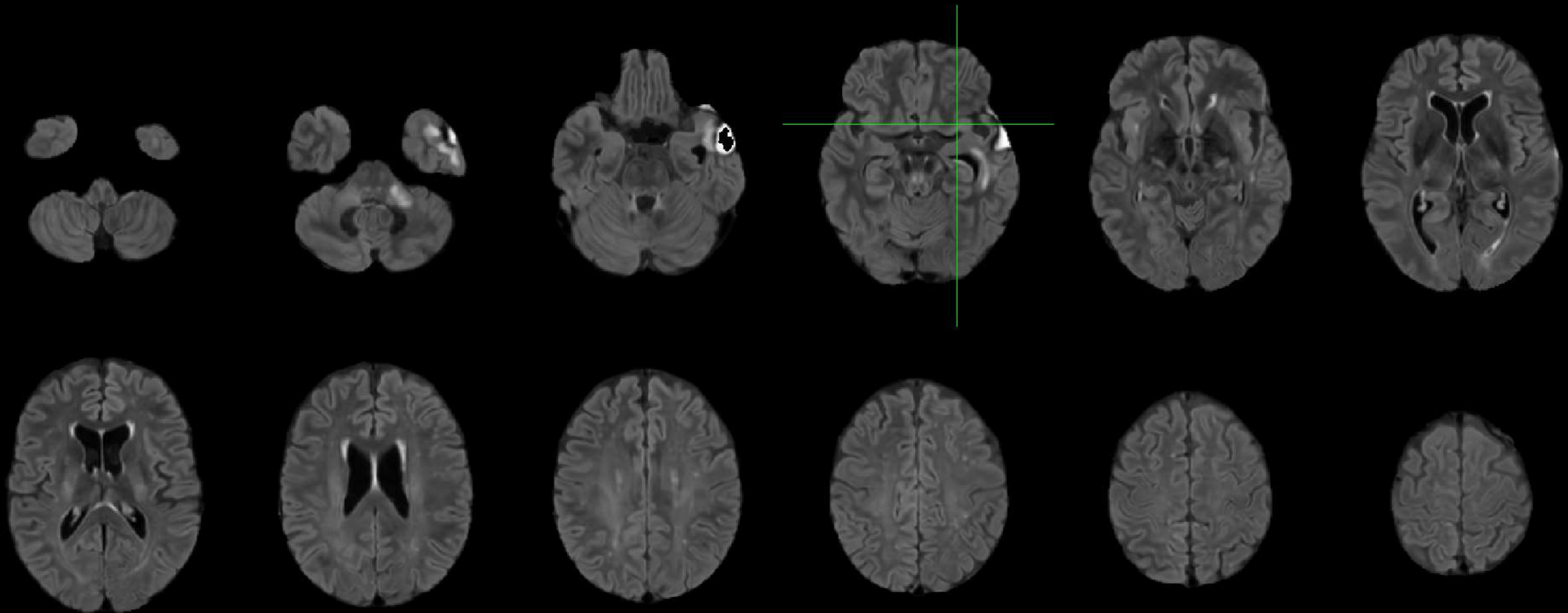


Burduja, Mihail, Radu Tudor Ionescu, and Nicolae Verga. "Accurate and efficient intracranial hemorrhage detection and subtype classification in 3D CT scans with convolutional and long short-term memory neural networks." *Sensors* 20.19 (2020): 5611.

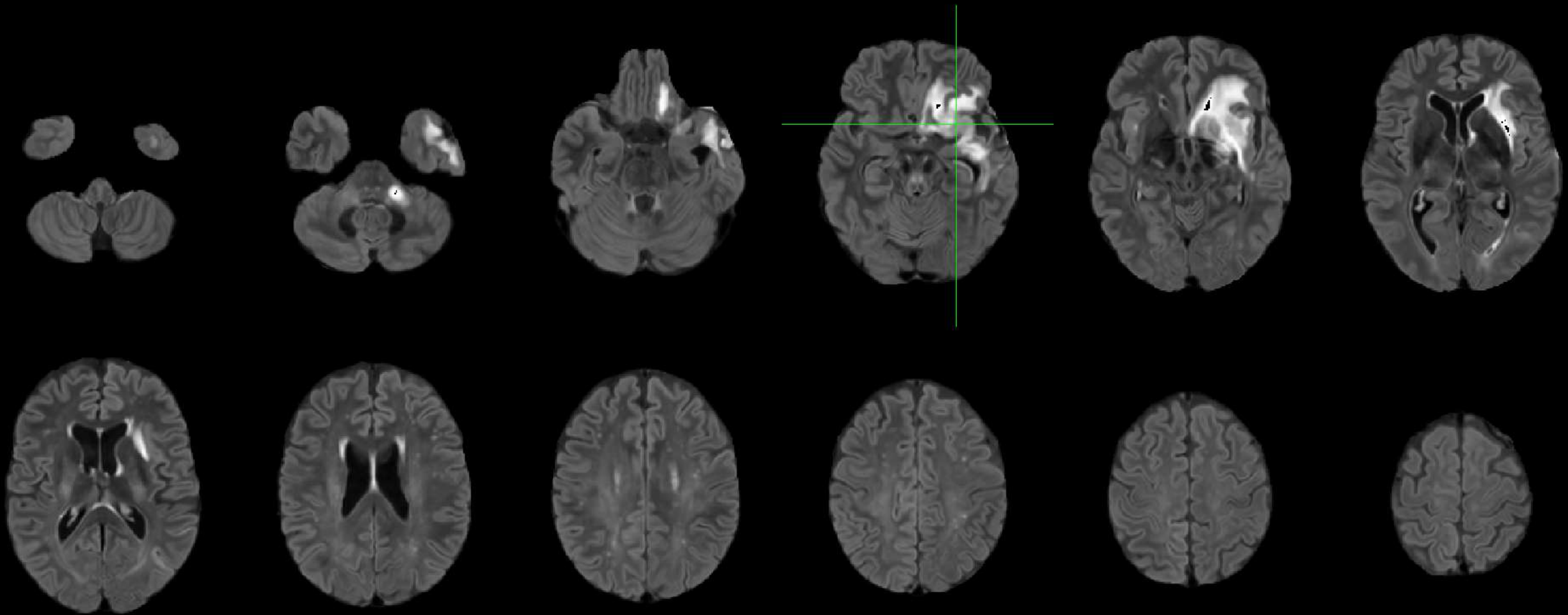
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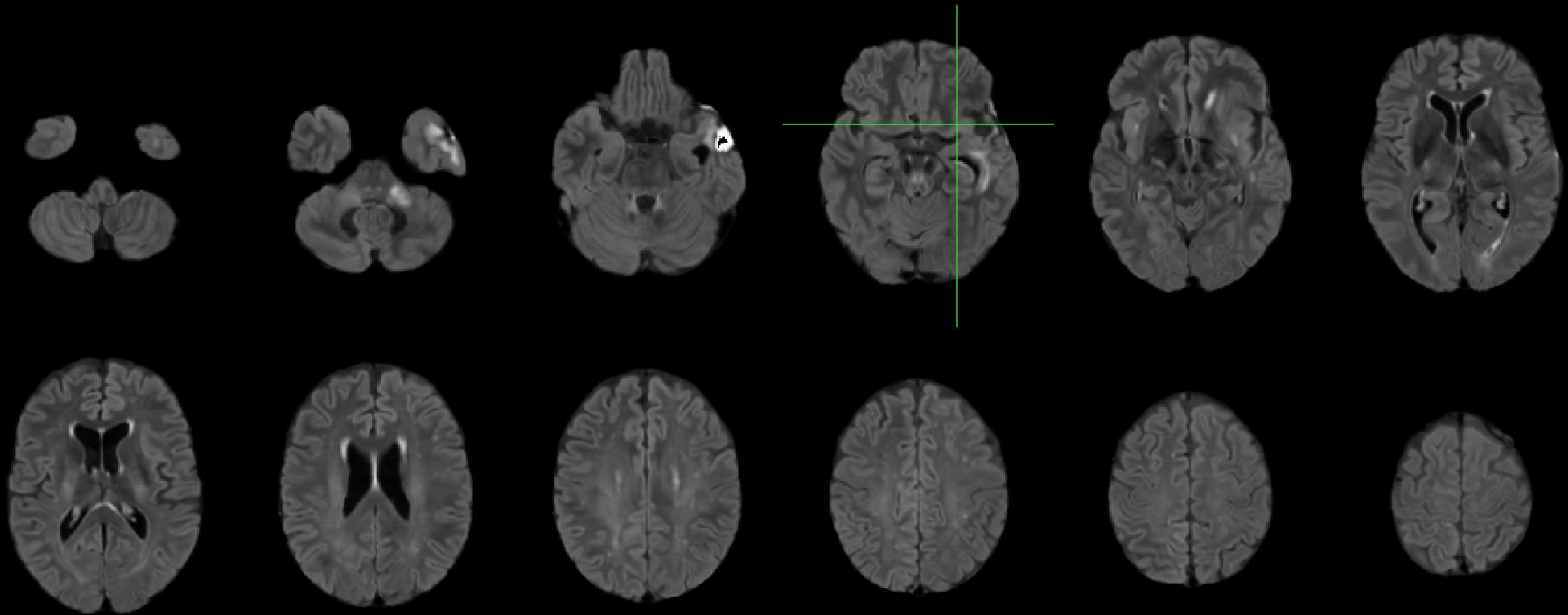
- Endring av vevsbit (voxel): forflytning + intensitetsendring
- Forflytning estimert fra deformerbar koregistrering
- Fordeler:
 - Bygger på forskning fra Elies F. Garcia om at estimert forflytning fra deformerbar koregistrering kan være tidlig markør for tilbakefall
 - Kan skille vekk forflytning mellom to tidspunkt slik at kun intensitetsendring analyseres med mer avanserte metoder



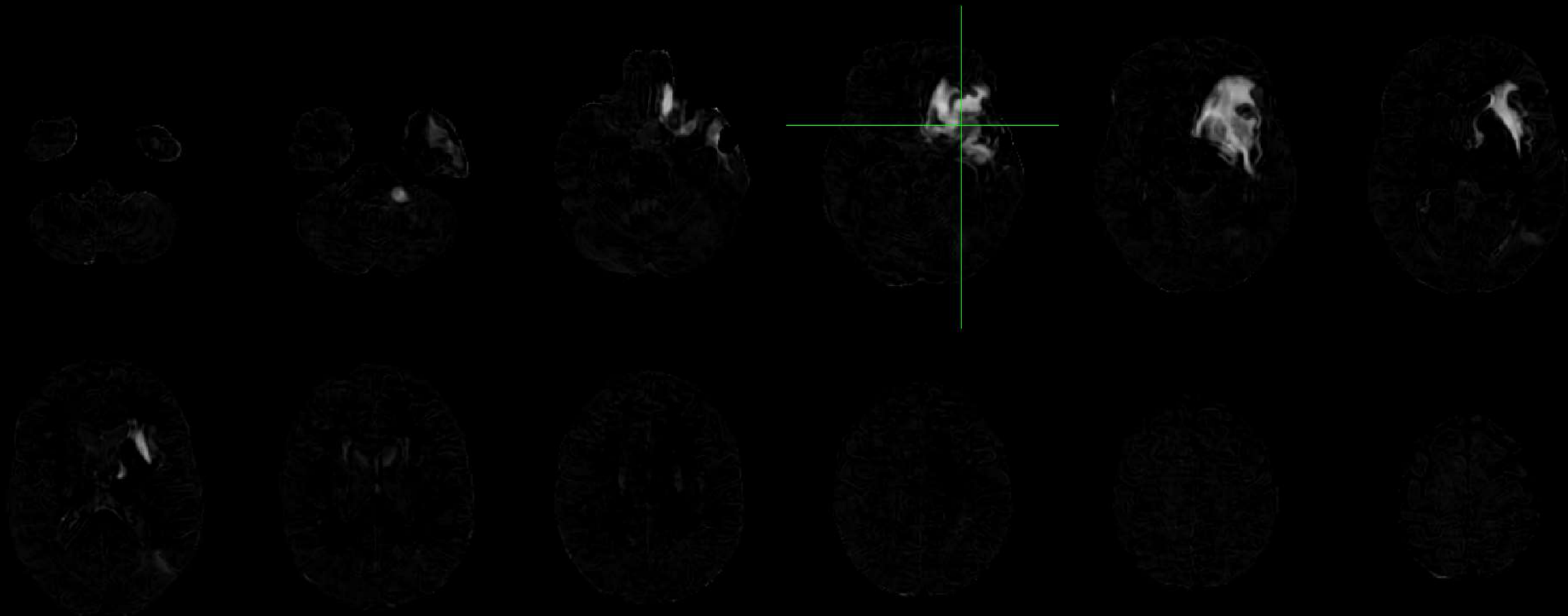
SAILOR, FLAIR, pas. 4, oppfølging 6



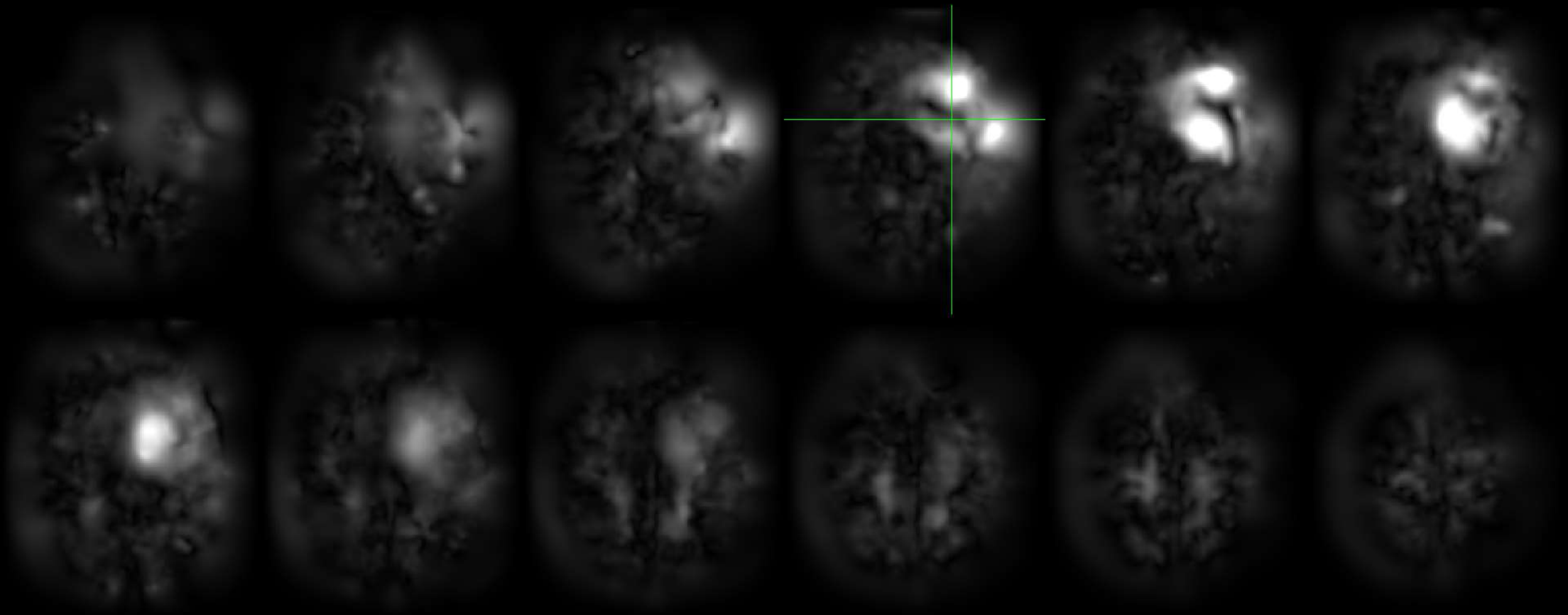
SAILOR, FLAIR, pas. 4, oppfølging 7



SAILOR, FLAIR, pas. 4, oppfølging 6 forflyttet til oppfølging 7



SAILOR, FLAIR, pas. 4, oppfølging 7 – (oppfølging 6 forflyttet til oppfølging 7)



Estimert forflytning fra ANTs SyN

3. Prediksjon av neste bilde basert på forflytning og intensitetsendring

- Endring av vevsbit (voxel): forflytning + intensitetsendring
- Forflytning estimert fra deformerbare koregistrering
- Ulemper:
 - Konkurrerer med etablerte metoder for kreftprediksjon (diffusion-reaction, bruk av DTI, etc.) *Falco, Jacopo, et al. "In Silico Mathematical Modelling for Glioblastoma: A Critical Review and a Patient-Specific Case." Journal of Clinical Medicine 10.10 (2021): 2169.*
 - Dataintensive dyp læring-baserte metoder

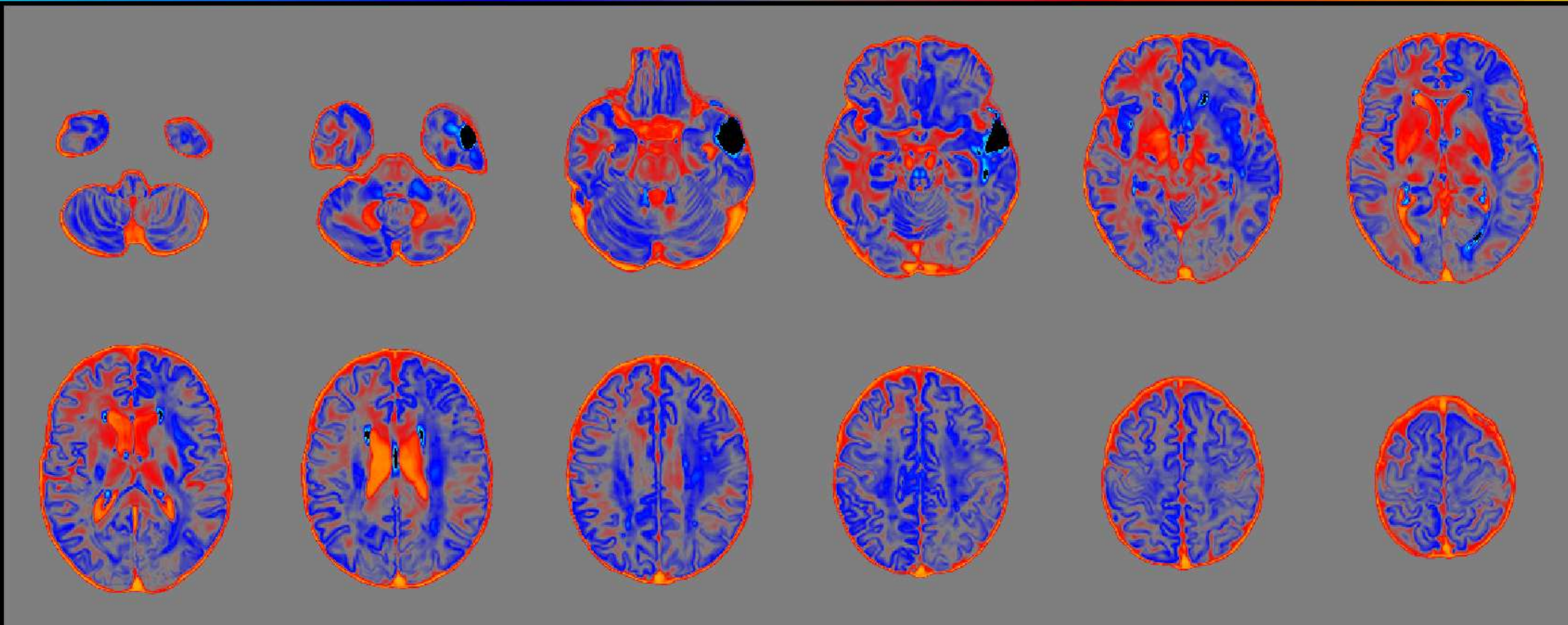
ConvLSTM: *Zhang, Ling, et al. "Spatio-temporal convolutional LSTMs for tumor growth prediction by learning 4D longitudinal patient data." IEEE transactions on medical imaging 39.4 (2019): 1114-1126.*

GANs: *Elazab, Ahmed, et al. "GP-GAN: Brain tumor growth prediction using stacked 3D generative adversarial networks from longitudinal MR Images." Neural Networks 132 (2020): 321-332.*

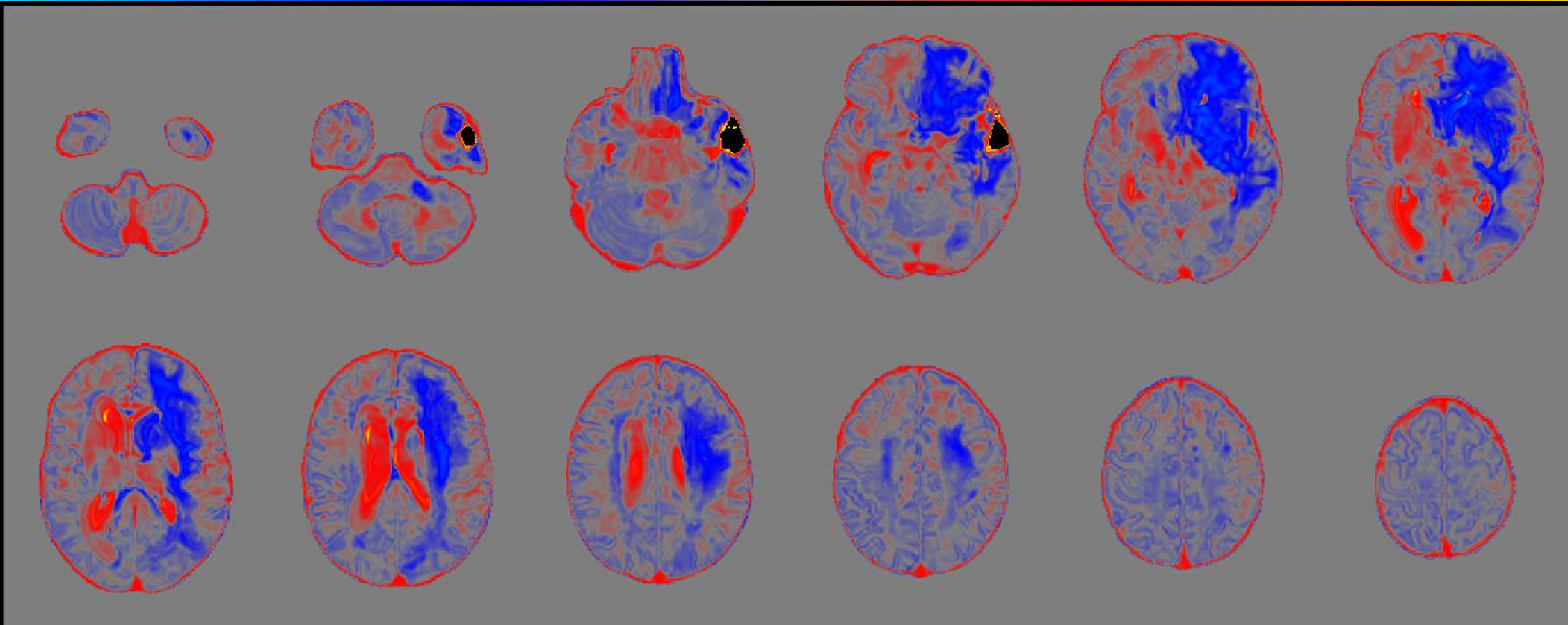
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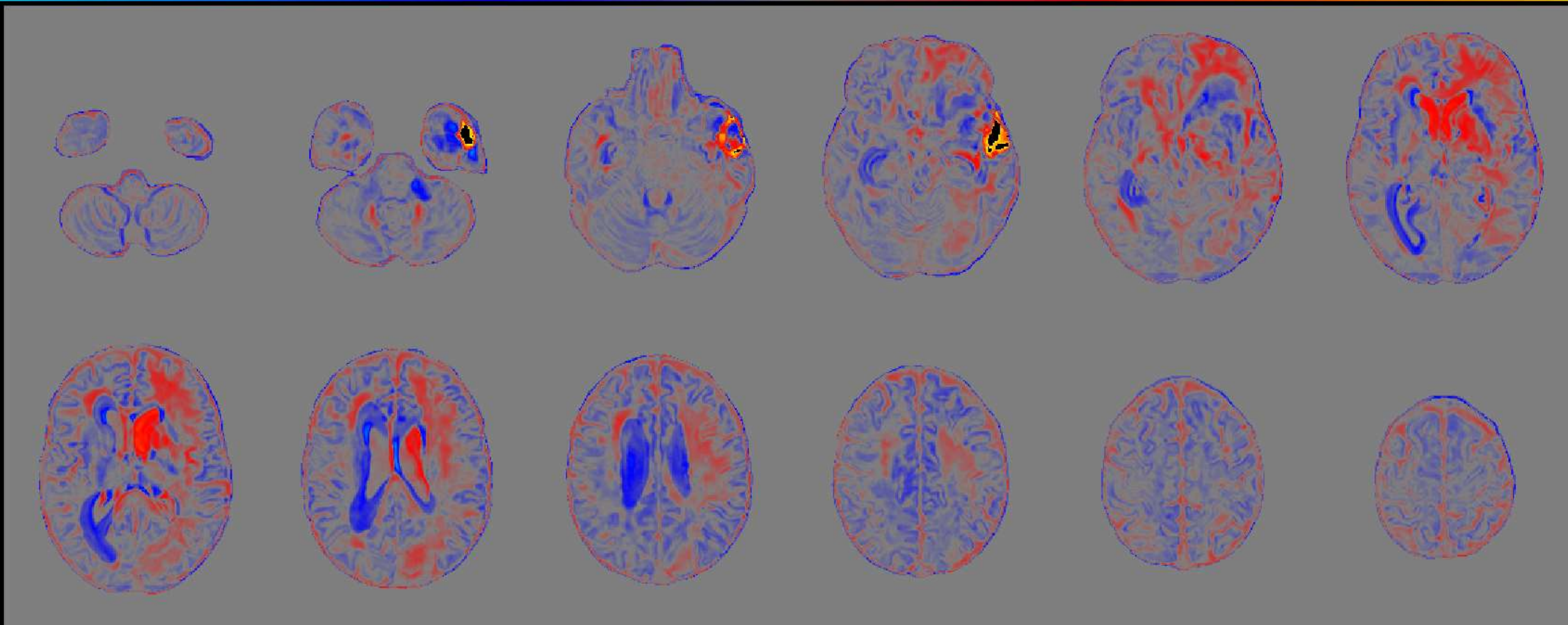
- Kan bruke uledete (unsupervised) metoder for å finne generelle mønstre i bilder på tvers av pasienter og tidspunkt. PCA, autoencoder, etc.
- Mapping av variasjonen av behandlingsforløp i «latent rom»
- Fordeler:
 - Kan fortelle hvor en ny pasient/scan hvor ligger i forhold til eksisterende pasienter som har fullstending behandlingsforløp
 - Grov prediksjon av behandlingsforløp basert på nærhet til klynger (clusters)
- Ulemper:
 - For generell modell til å fortelle noe om enkeltpasienter
 - Kobling mellom klynger og kliniske parametre (tumorvolum, alder, etc.)



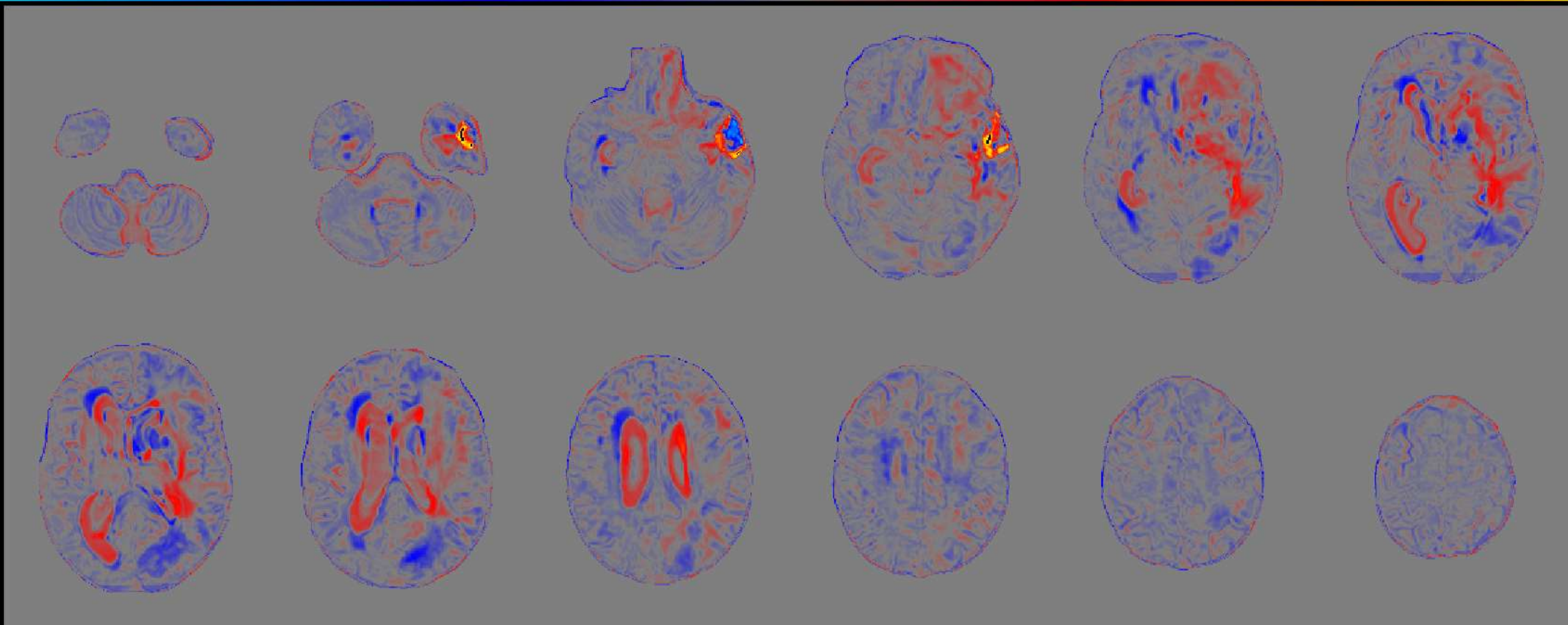
Prinsipalkomponentanalyse (PCA) av SAILOR, FLAIR, pas. 4



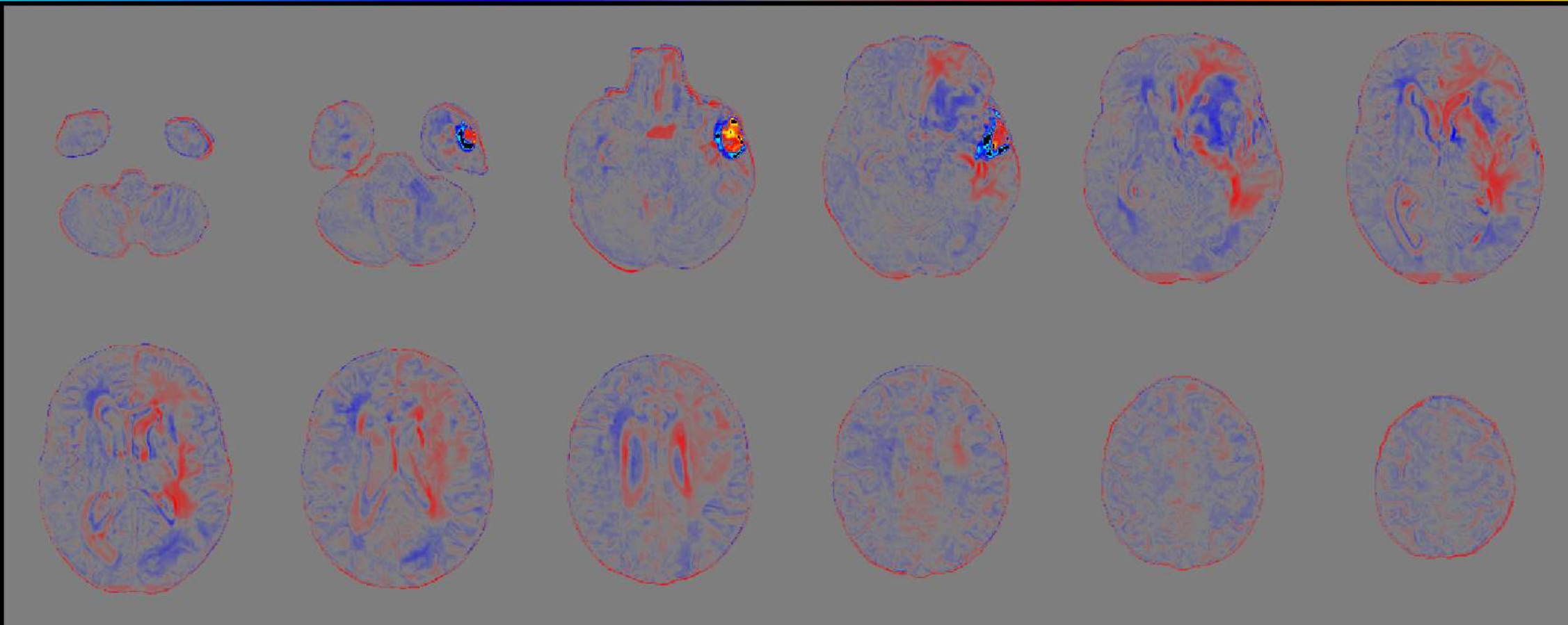
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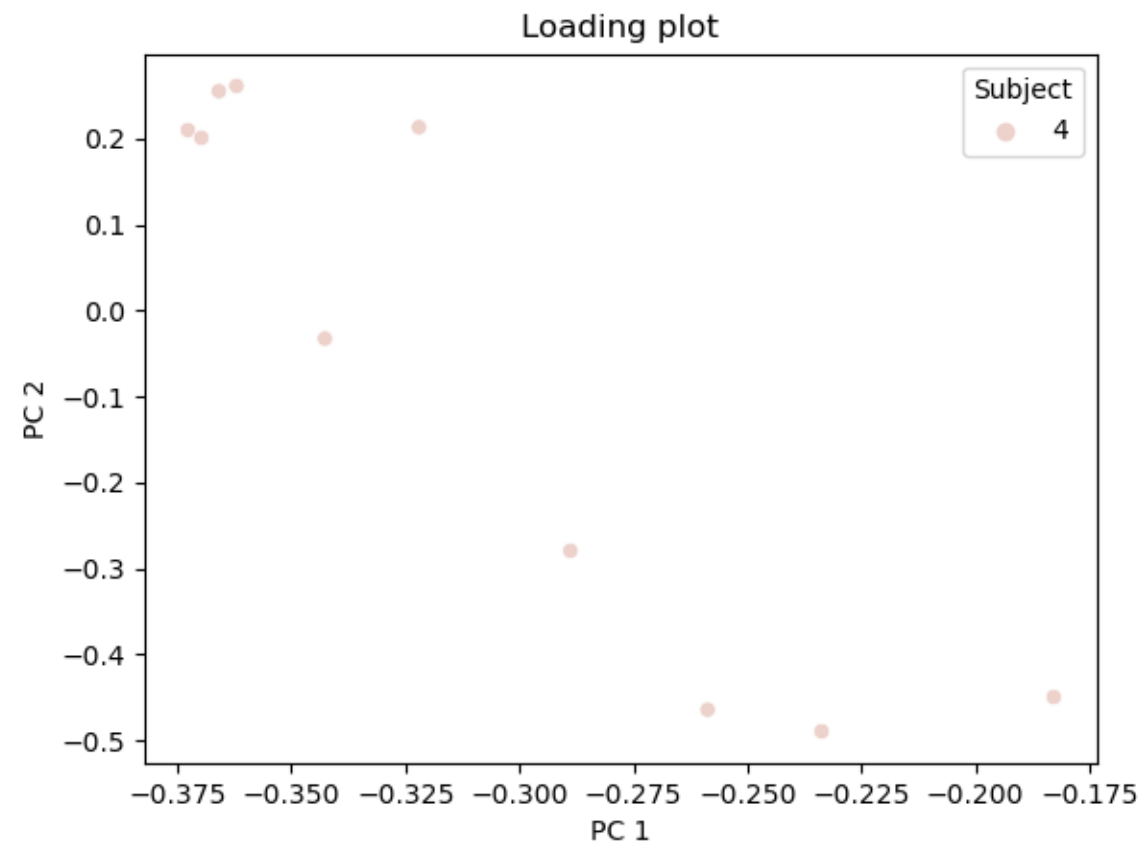
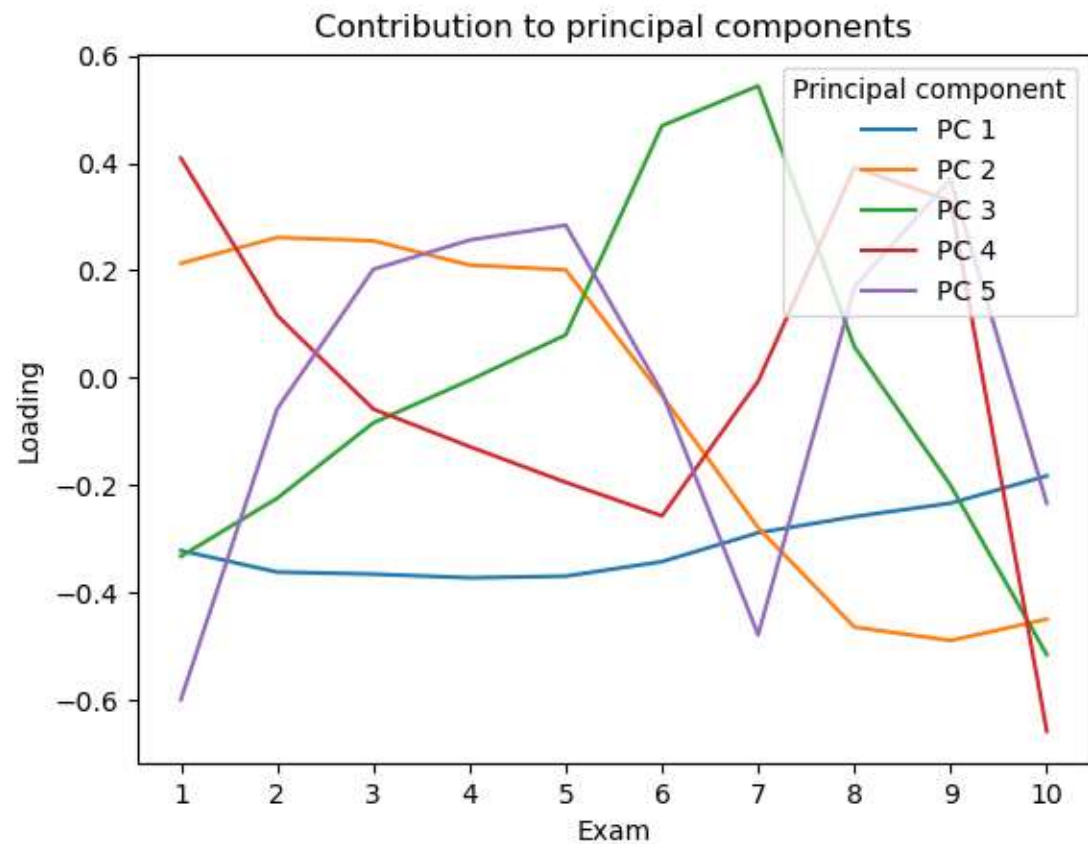
Prinsipalkomponentanalyse (PCA) av SAILOR, FLAIR, pas. 4



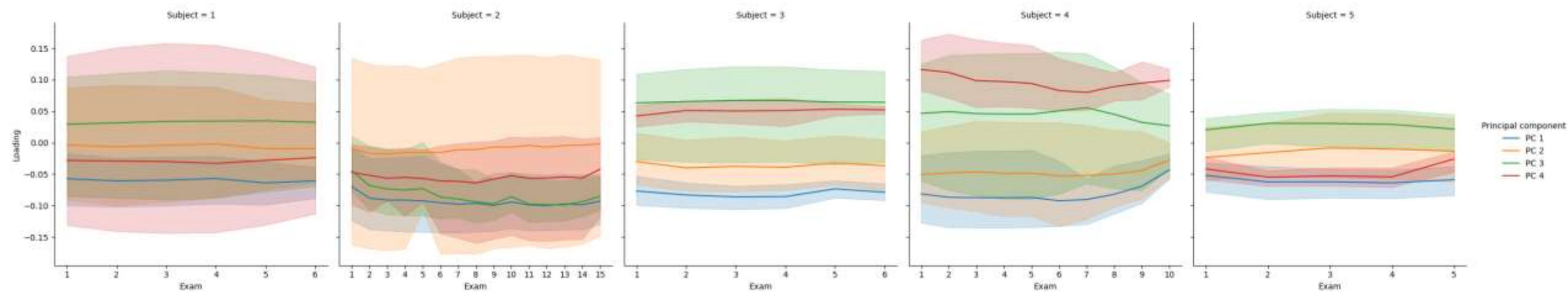
Prinsipalkomponentanalyse (PCA) av SAILOR, FLAIR, pas. 4



Prinsipalkomponentanalyse (PCA) av SAILOR, FLAIR, pas. 4

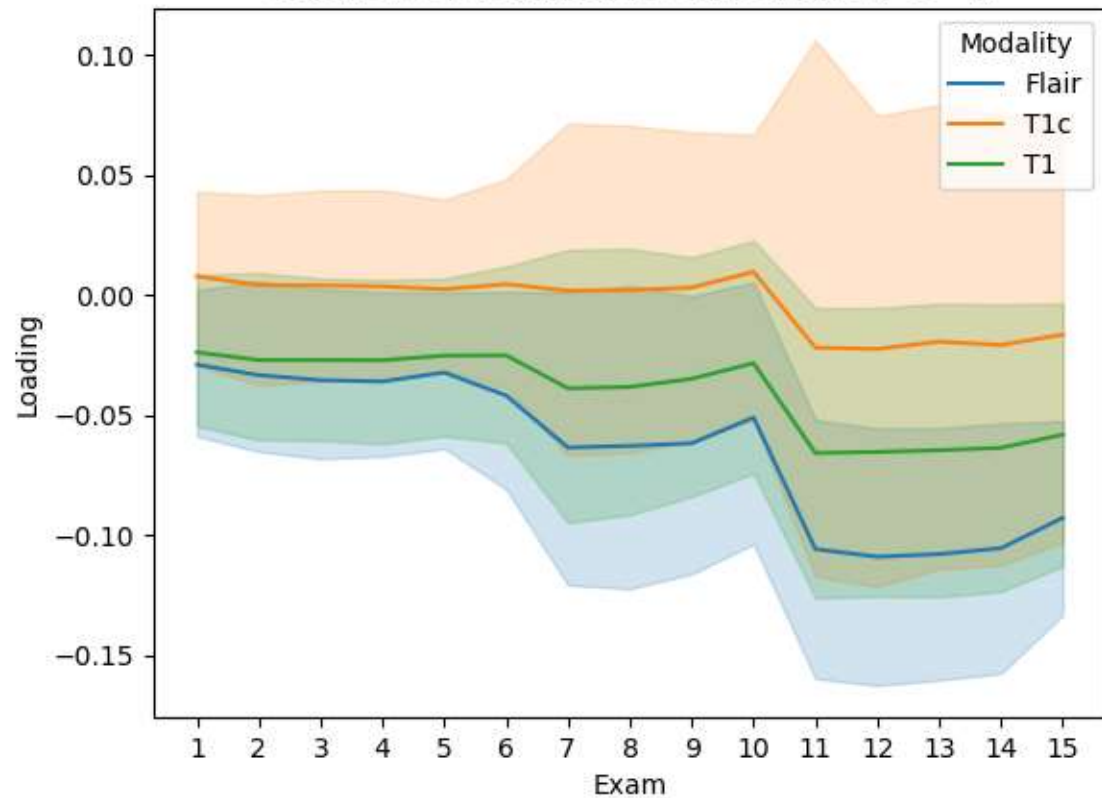


Prinsipalkomponentanalyse (PCA) av SAILOR, FLAIR, pas. 4

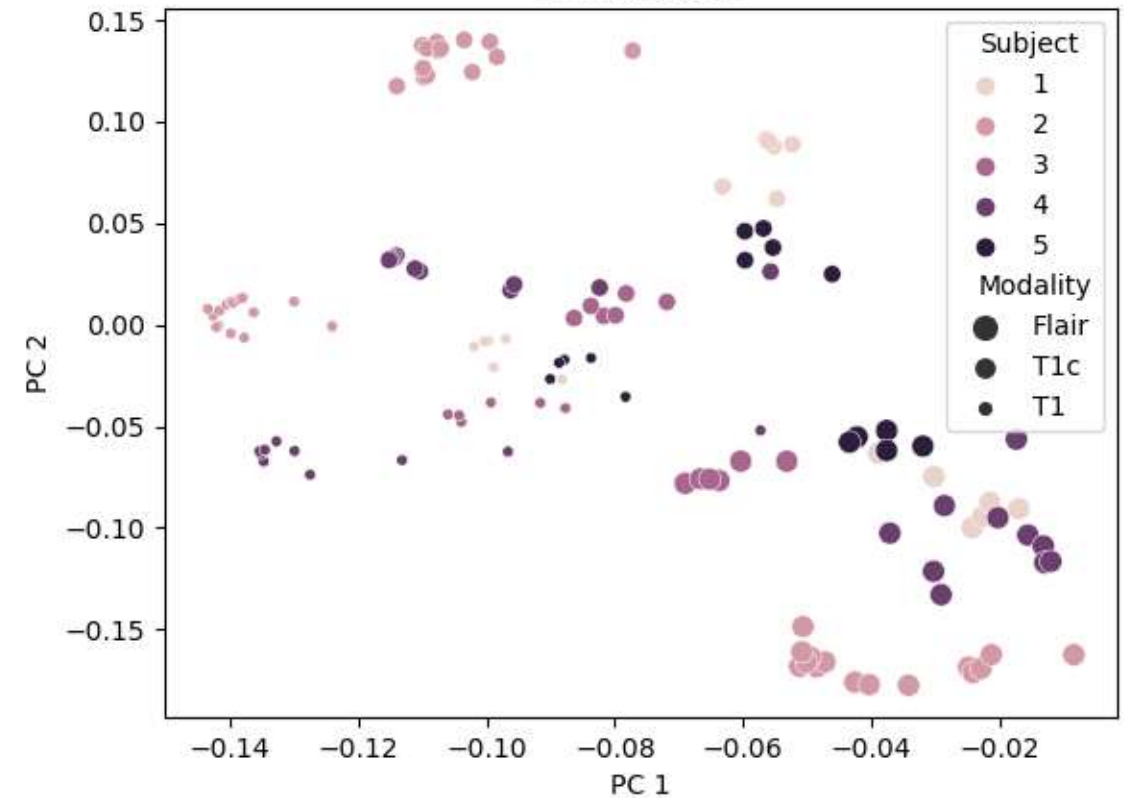


Prinsipalkomponentanalyse (PCA) av SAILOR, T1, T1c, FLAIR, pas. 1-5

Contribution to principal components (PCs=4)



Loading plot



Prinsipalkomponentanalyse (PCA) av SAILOR, T1, T1c, FLAIR, pas. 1-5

PCA shape components

- 😊 Easy to **visualize**.
- 😞 Just summarizes data variability → they **do not** necessarily encode anatomical features that can **differentiate** between classes.

Machine Learning approaches

- 😊 Powerful feature extraction.
- 😞 Lack interpretability

(Variational AutoEncoder)
➡ VAE

Learns a set of latent variables z that:

1. can **differentiate** clinical conditions y .
2. and whose anatomical effect can be **visualized**.