Quantitative MR, Promising Data as a Replacement of CT

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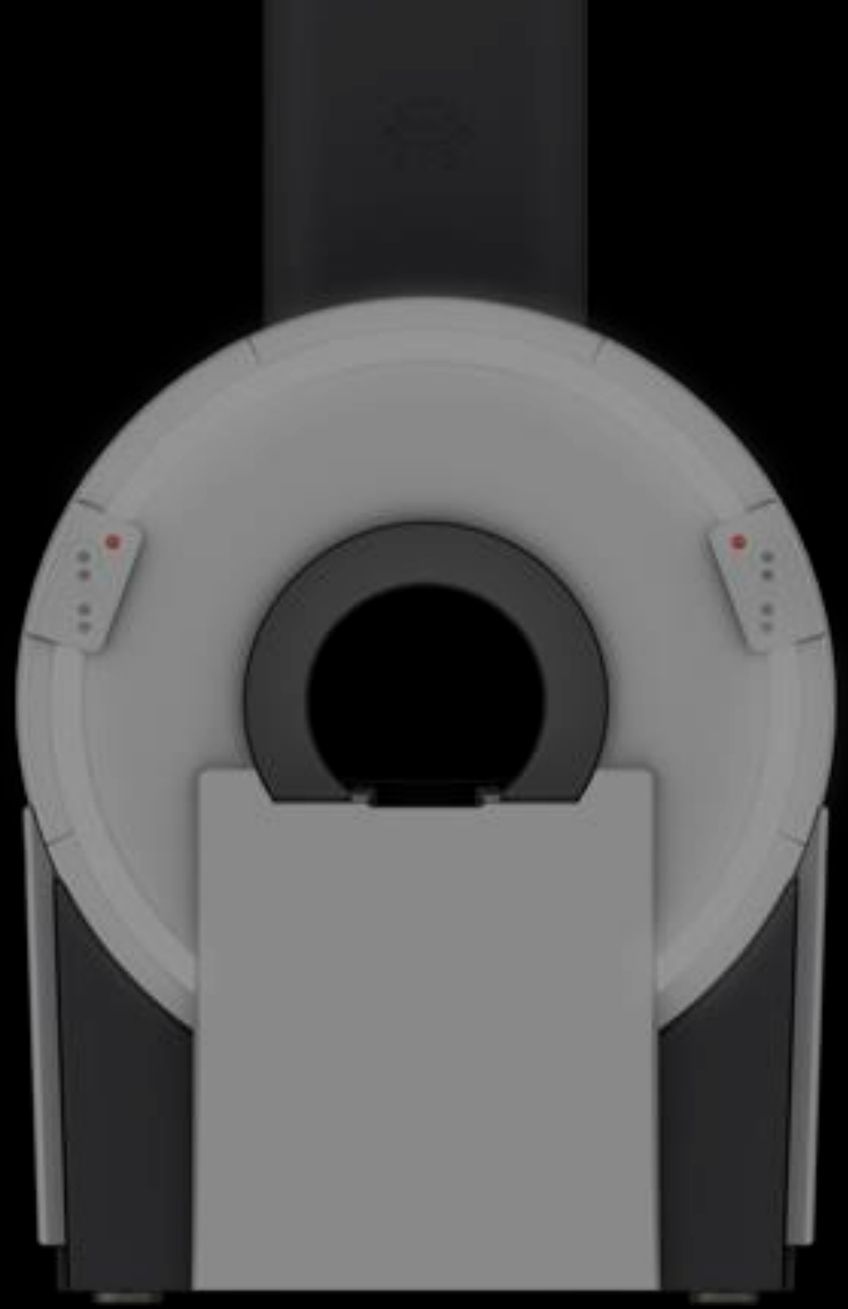
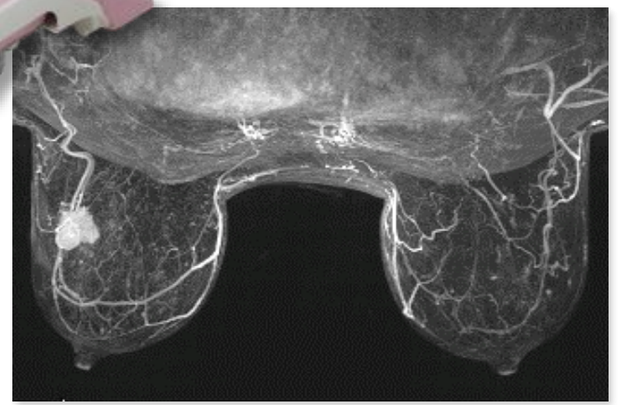
President/CTO Synaptive Medical

March 12 2025



Introduction to MRI as a replacement for X-ray

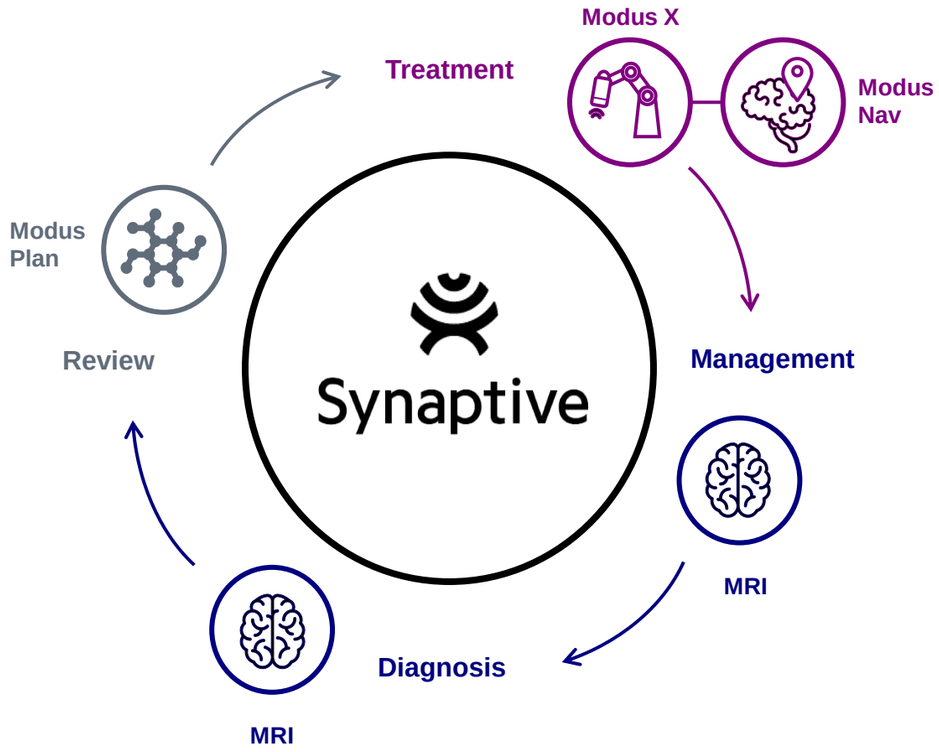
- Founding team of Synaptive from Sentinelle Medical
- Engineers and physicists **enhancing the power of MRI**
- Focused on breast cancer detection and therapy
- Expanded from screening to interventional guidance and therapy delivery
- **MRI is the "Gold Standard," potential is enormous**



MRI has the most significant value when used across the patient care cycle

A Toronto-based, global medical device and technology company (full vertical) delivering precision imaging and interventional platforms to guide precision therapy

Addressing critical clinical needs in the operating room and beyond by enabling an imaging first approach to automation and robotic surgery



Broad and accelerating utilization in surgery, radiation therapy, stroke intervention (ischemic and hemorrhage), drug-infusion monitoring and a broad variety of device implantations (deep-brain stimulation, pain stimulators)

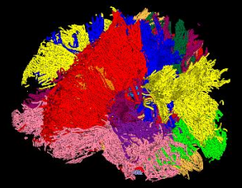
These are all venues where MRI is displacing CT

One of the founders of INOVAIT Program

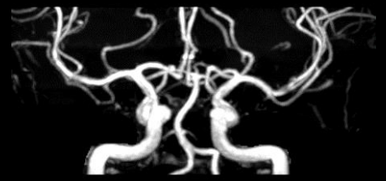
Matrix of Imaging to Provide Stereotactic and Surgical Guidance

Synaptive 0.5T MRI

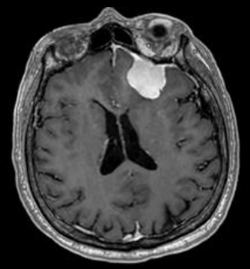
Neurons / Connectivity



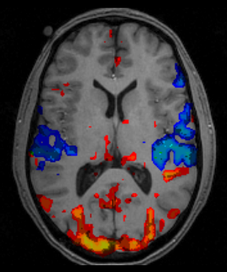
Blood Vessels



Clot, Tumor, Disease



Function, Thought



"In acute care where every second counts, having the ability to clearly visualize and diagnose patients is critical for maximizing patients' chances of success. … healthcare professionals now have an added tool that will allow for more informed decision-making in situations where MRI is not feasible"

Dr. Taufik Valiante, Toronto Western Hospital

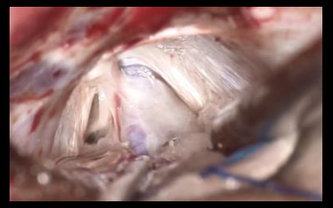
UNIVERSITY OF TORONTO

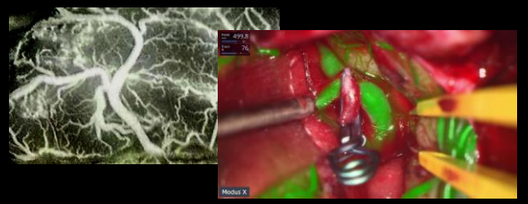
"There have been times that our images were better than the patient's previous imaging so much so that the patient treatment planning was changed… a patient with 4 Mets that ended up having 20+ when they scanned in the Synaptive MRI"

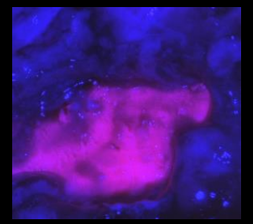
-Dr. Tim Chen South Jersey Meriden Health

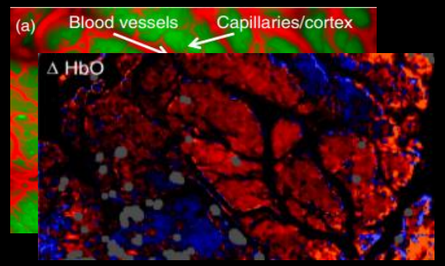
Hackensack Meridian *Health*

Modus X









"The Synaptive exoscope is an example of a disruptive tool that makes surgery better for our patients and is ergonomically superior for the surgeon."

-Dr. Theodore, neurosurgeon at Johns Hopkins

JOHNS HOPKINS MEDICINE

"It is exciting to see a company take on the immense challenge of truly innovating in surgical medicine rather than settling for minor variations of existing technologies."

-Dr. Vargo, Cranio-facial Plastic Surgeon Children's Nebraska

Children's HOSPITAL & MEDICAL CENTER OMAHA

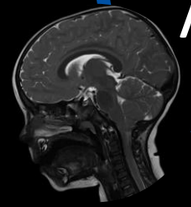
Better visualization leads to definitive improvements in patient care and clinical-economics metrics

Environment: Applications for Neuro MRI are Rapidly Expanding displacing CT

- MRI information is the most valuable data for neuro conditions. Without MRI advanced treatments are not possible
- Capacity in the USA is currently **only 40M MRI Scans/yr** (all applications), while excluding many in need
- Demand for new neuro applications will exceed MRI capacity. **Alzheimer's infusions alone require 35M scans** (1)
- Global installation base to meet USA per capita MRI capacity needs to increase from 50K systems to 250K systems

Limited MRI access is restricting some of the most impactful therapies in a $1T y/USD US market today

Developmental / Pediatric

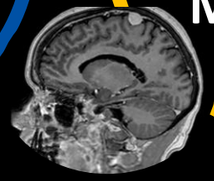


12M Developmentally Impaired Children

Future State:
350M / yr to benefit from yearly screening

CT now restricted due to radiation concerns MRI must fill void

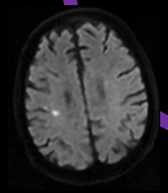
Tumor / Primary & Metastatic



280K new patients / yr (Primary and Metastatic)

MRI is cornerstone for detection, monitoring, staging and guidance

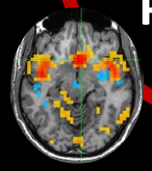
Acute Care / TBI, Stroke & Vascular



2.5M new patients / yr (Vascular Intervention, ICH Surgery)

MRI detects all strokes, CT misses 25%

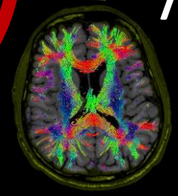
Behavioral / Neurology/ Psychiatric



60M+ patients (Repeat TMS, Drug Delivery)

Functional MRI and DTI used for diagnosis and stimulation targeting (TMS)

Degenerative / Functional



7M patients (AZ,MS) (Screening, Infusions)

3.3M patients (Deep Brain Stimulation, Epilepsy, Drug Delivery)

New Alzheimer's drugs require 5 MRI scans per course for safety monitoring
MS Infusions require serial MR

(1) FDA requirement of 5 MRI scans needed in parallel with Drug Infusions (2) MRI of Stroke: Diagnostic Accuracy 0.5/1.5/3.0 CT Wagner et all, 2022

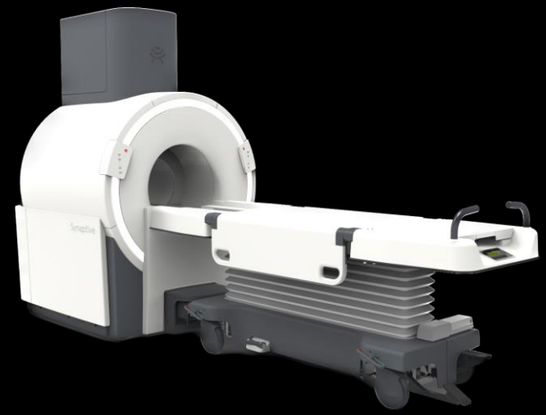
Revolutionary Design Required to Address the Needs of Today

Synaptive MRI was developed from ground up to address unmet challenges of MRI access and intervention

- **Incumbent imaging systems have not yet evolved** from traditional radiology service focus to therapy delivery platforms
- Critical specialties (Surgery, Radiation Therapy, Neurology, Stroke Intervention, Pediatrics, Geriatrics) needs have not been prioritized
- Patient care pathway from screening, diagnosis and therapy delivery is poorly addressed and not scalable. This issue is amplified globally

Legacy MRI Systems (1.5T – 3.0T Field)

- **High** capital investment, operation, and construction costs
- **Massive** Size: 20,000+ lbs. weight, 1,000 sq-ft room
- Helium Fill and Venting Required, **always on**
- Claustrophobic, Heating, No Devices **(reduced access)**
- **Poor reproducibility, quantitative results, spatial accuracy**



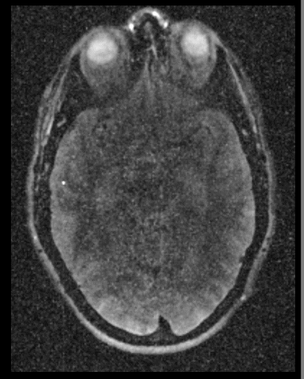
Synaptive Head-Only MRI (0.5T)

- **Lower capital investment**, Much lower operation and construction
- **Smaller Size**: 4,000 lbs. weight, 250 sq-ft room
- No Helium, **can be turned on-off (15mins)**
- Significantly **better experience, access and device inclusion**
- **Excellent reproducibility, quantitative and spatial accuracy**

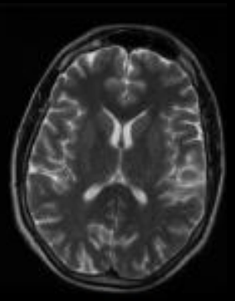
Imaging Progression

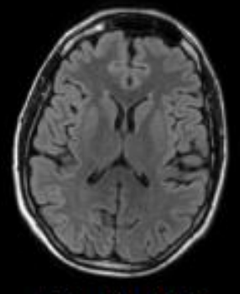
2016

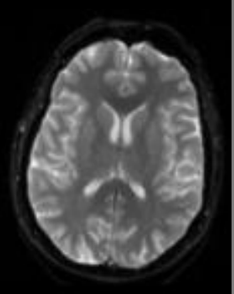

T1

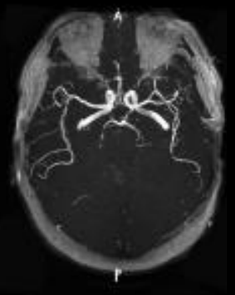

T2

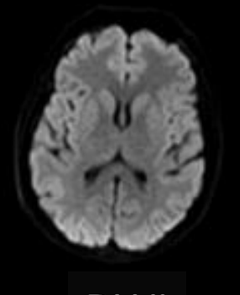
2019

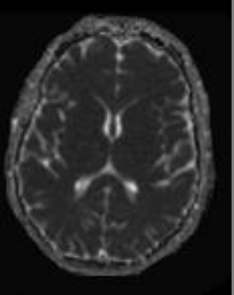

T2

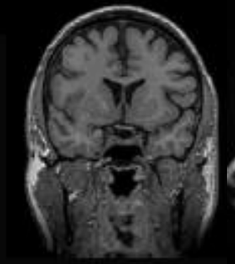

T2 FLAIR


T2*

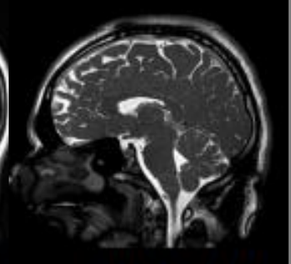

TOF


DWI

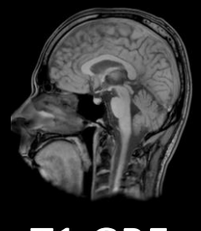

ADC

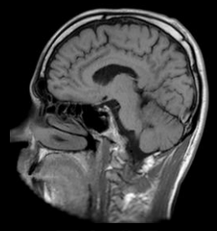

3D T1

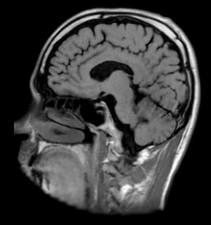

T1 FLAIR


3D SSFP

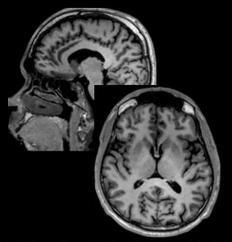
2025

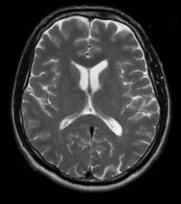

T1 GRE


T1 SE


T1 FLAIR


3D T1


3D MPRAGE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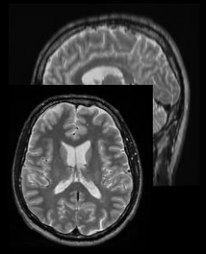
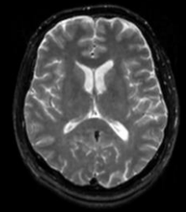
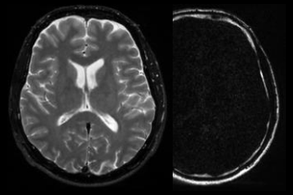

3D T2


T2 EPI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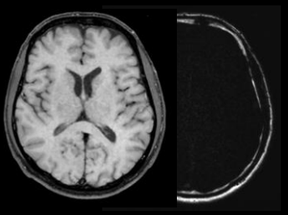
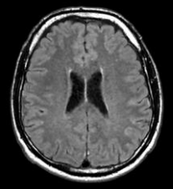

2D T1 CSE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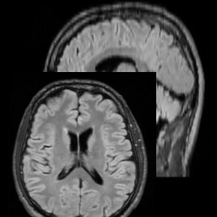
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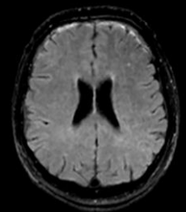
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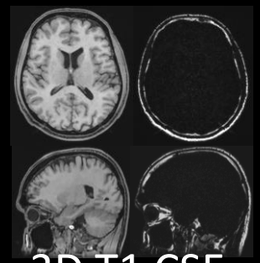
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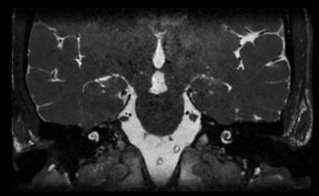
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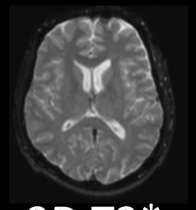
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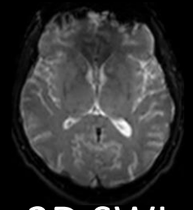
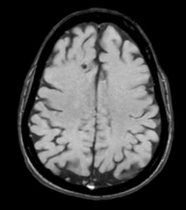

2D SWI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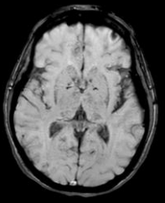
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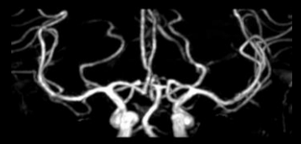
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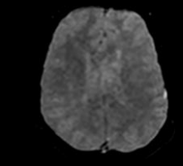
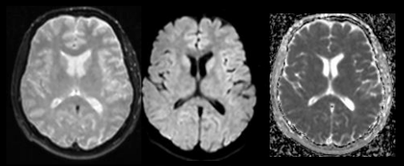

DSC-Perfusion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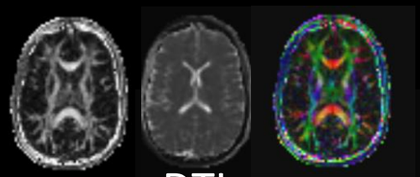
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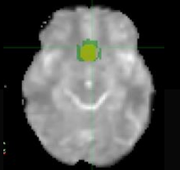
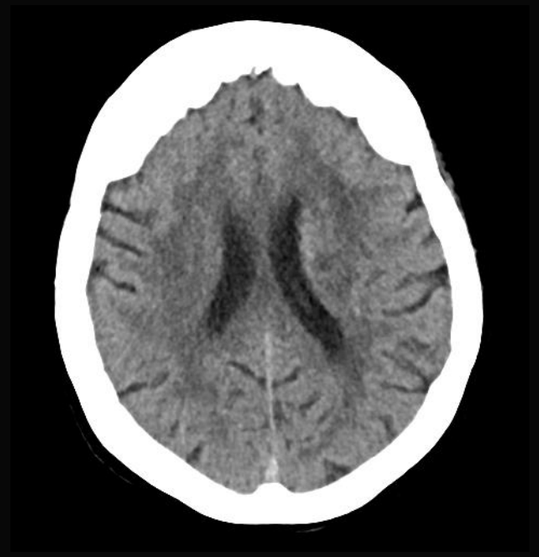

fMRI

Synaptive: MRI for Acute Stroke Care

CT – Standard of Care

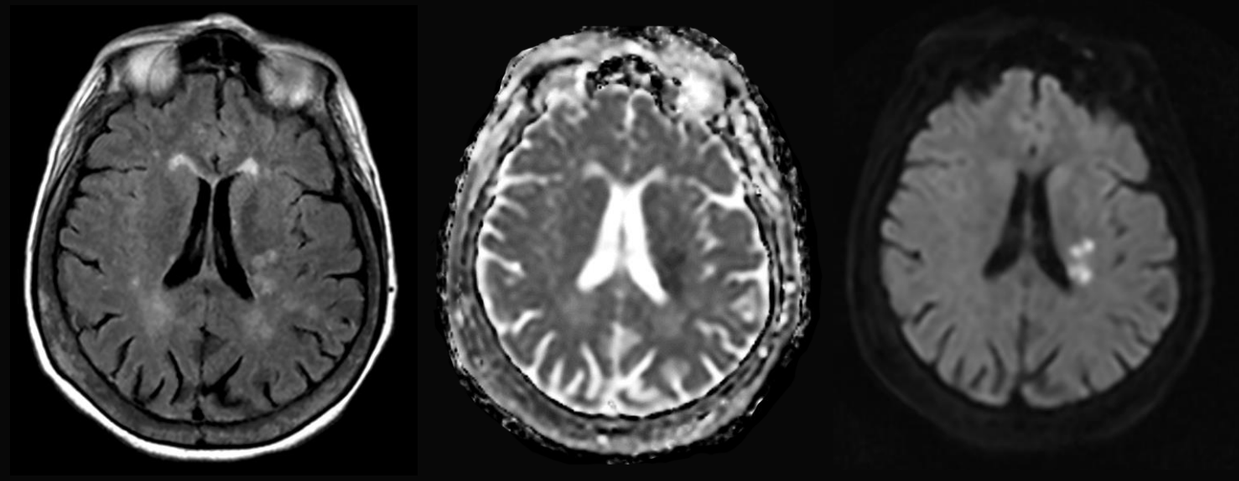


Synaptive MRI Compares very well to 1.5/3.0T for stroke detection

Synaptive MRI & 1.5/3.0T detect all strokes, where **CT misses 25% of clinical strokes**

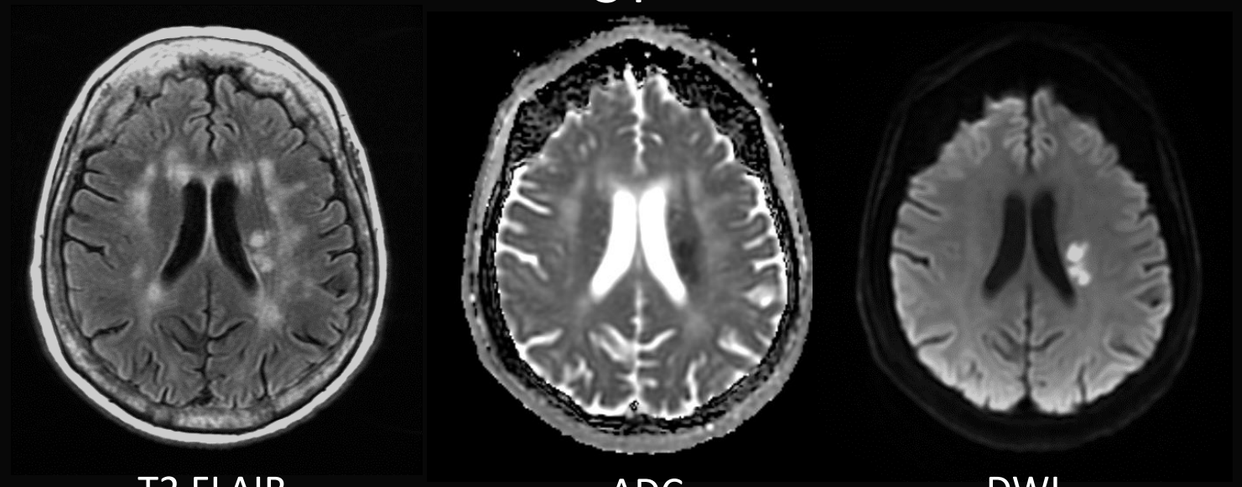
Increase in patients detected and helped

Synaptive 0.5T



T2 FLAIR **ADC** **DWI**

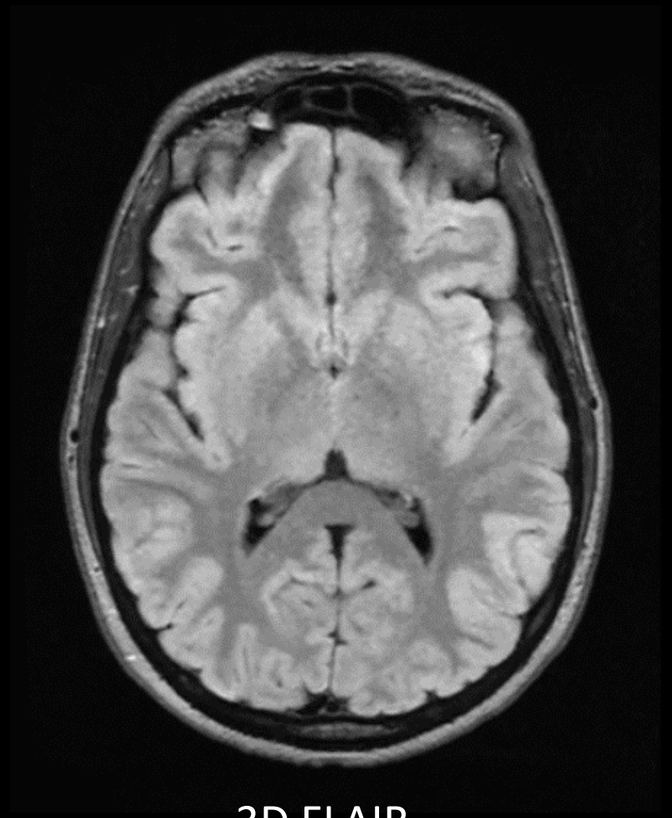
3T(1)



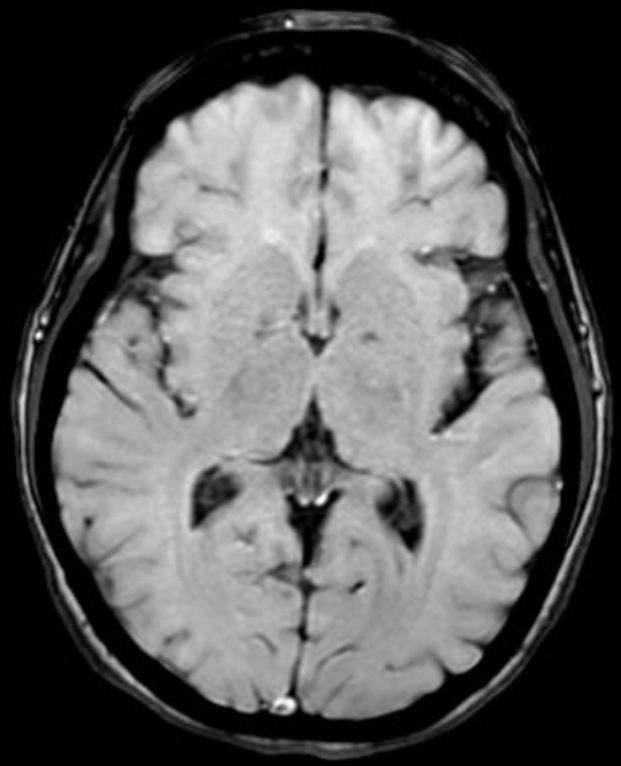
T2 FLAIR ADC DWI

(1) 3T is the highest-powered magnet for comparison.

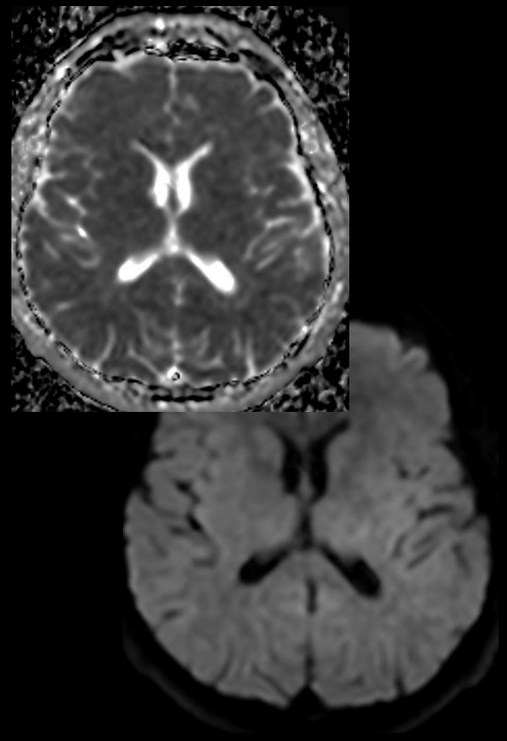
Typical Scan times for stroke evaluation



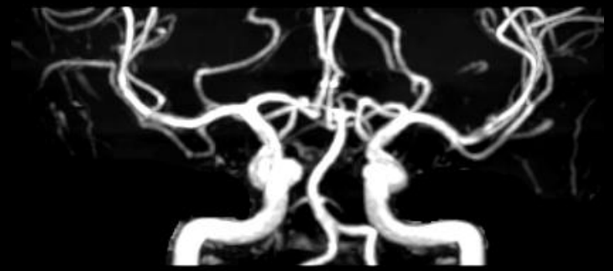
3D FLAIR
1 x 1 x 5mm
1:58



3D T2*w
1 x 1 x 3mm
5:05



DWI b=1000
1 x 1 x 5mm
1:37

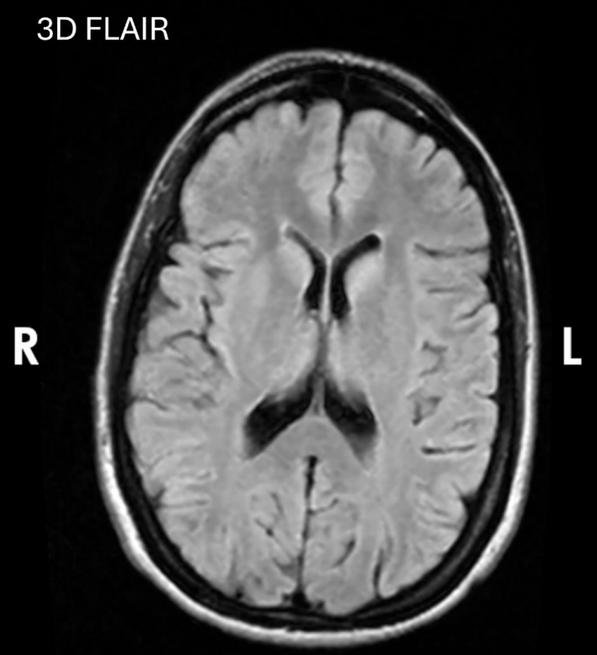


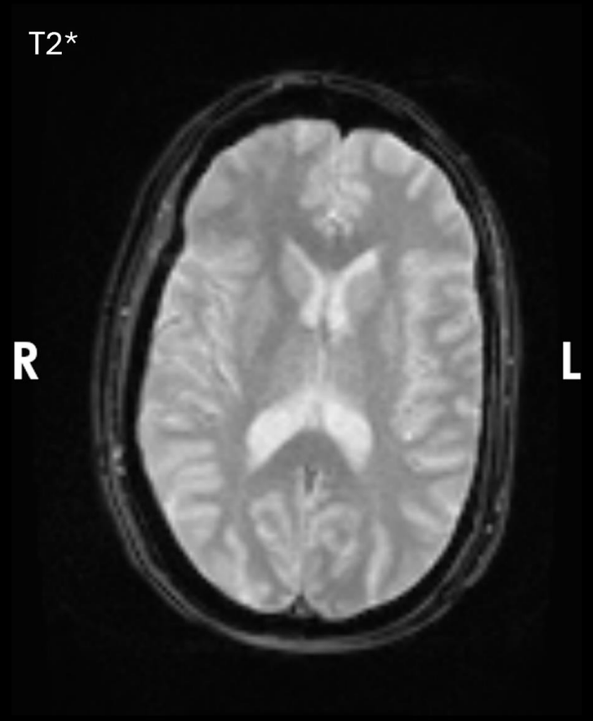
0.8 x 0.8 x 1mm, 72mm
slab, Scan time = 7:34

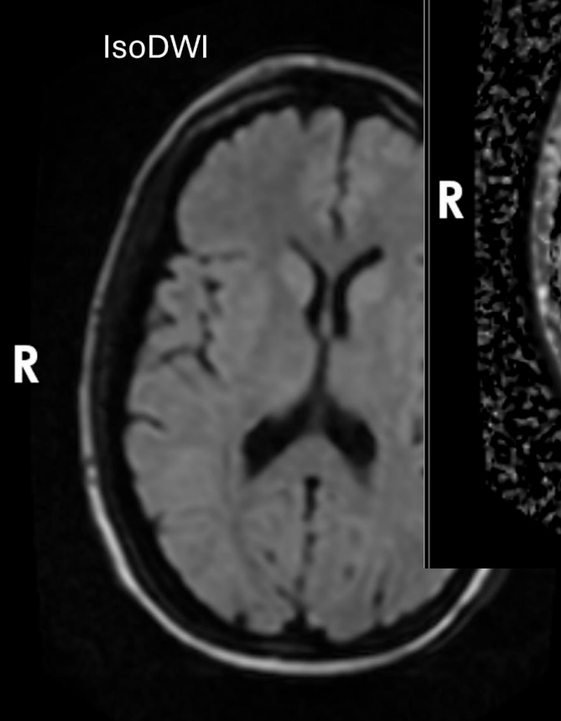
8:40

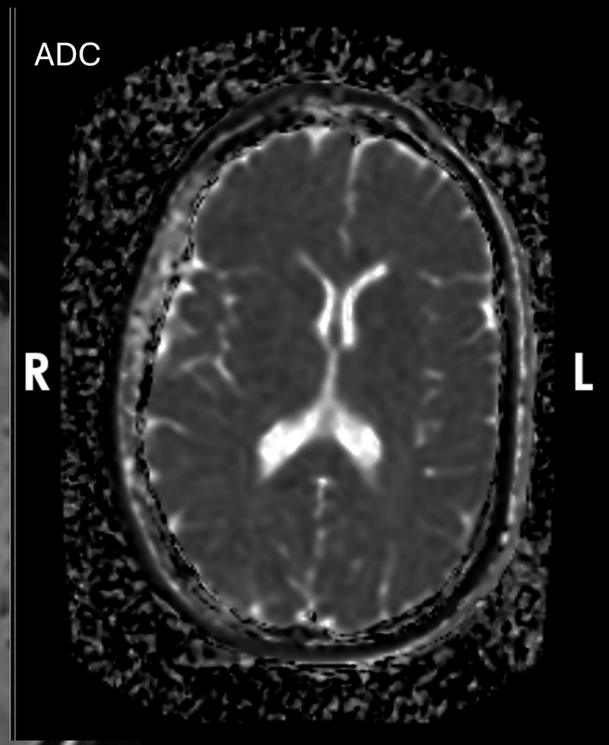
16:14

Ultra Accelerated Stroke Protocols









3D FLAIR
1 x 1 x 5mm
1:54

3D T2*w
1.5 x 1.5 x 5mm
58 sec

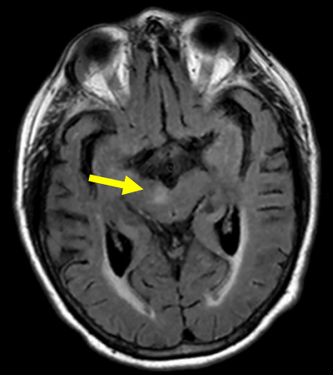
DWI b=1000
1 x 1 x 5mm
1:12

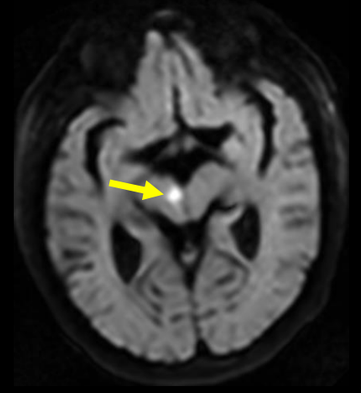
Potential For Additional:
2 Time Acceleration using AI
8 Time Acceleration using Compressed Sensing

4:20 Total Scan Time
10 min total Patient In-Out Time

Economic Benefits of MRI for Acute Stoke

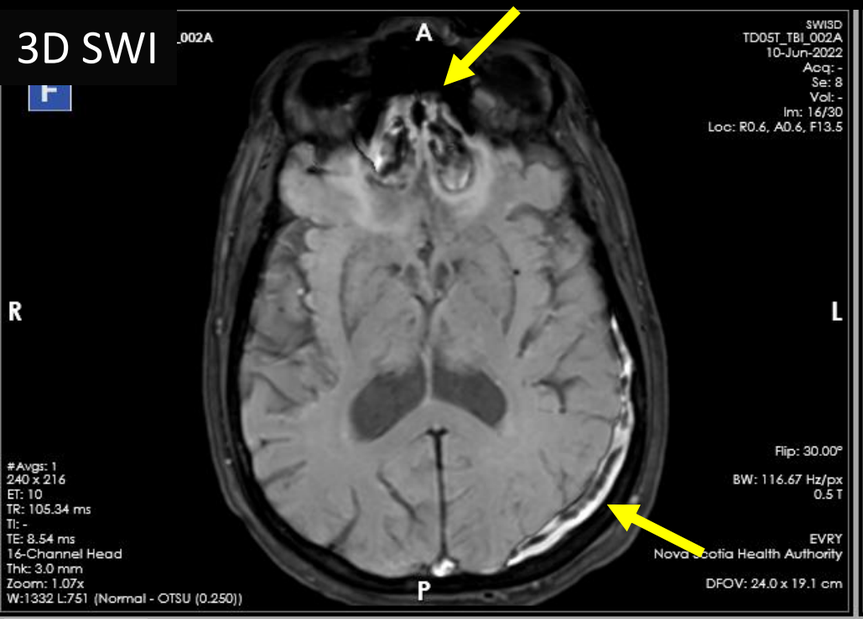
- Research in progress at Dalhousie University shows that access to MRI for acute stroke (2000 patients):
  - Reduces Length of Stay by 4 days
  - Reduces System Cost by 15%
  - Improves Patient Outcomes
- Furthermore, research also shows that performing the MRI as soon as possible can also increase the benefits

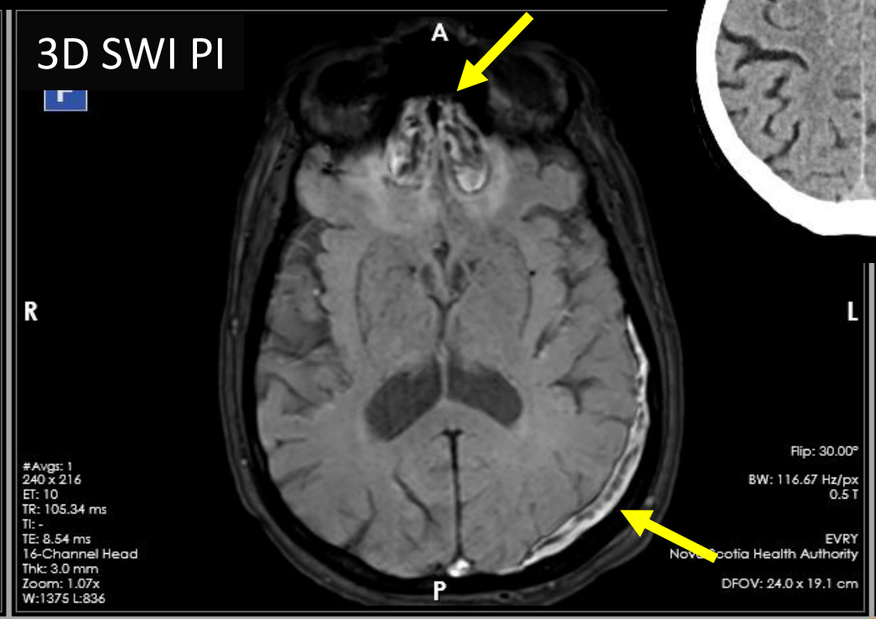


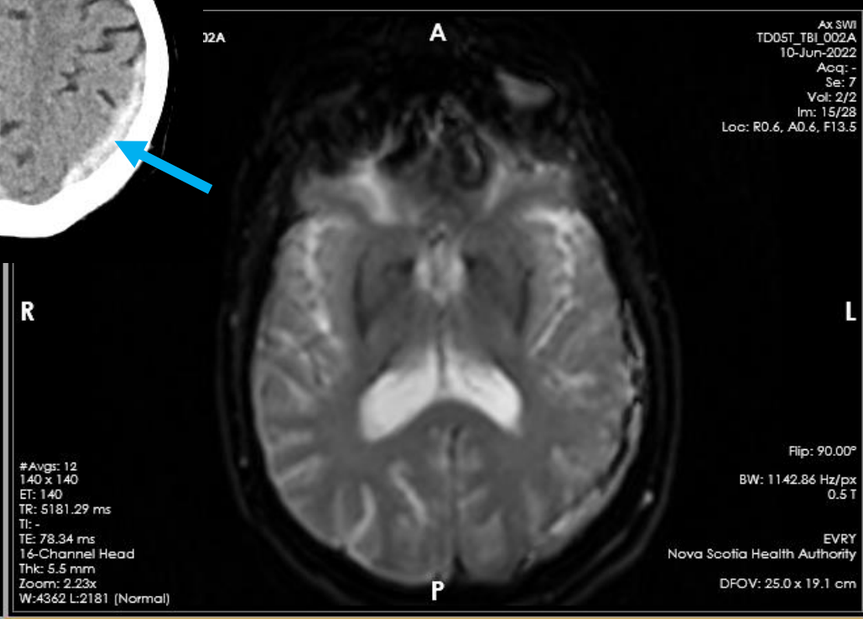


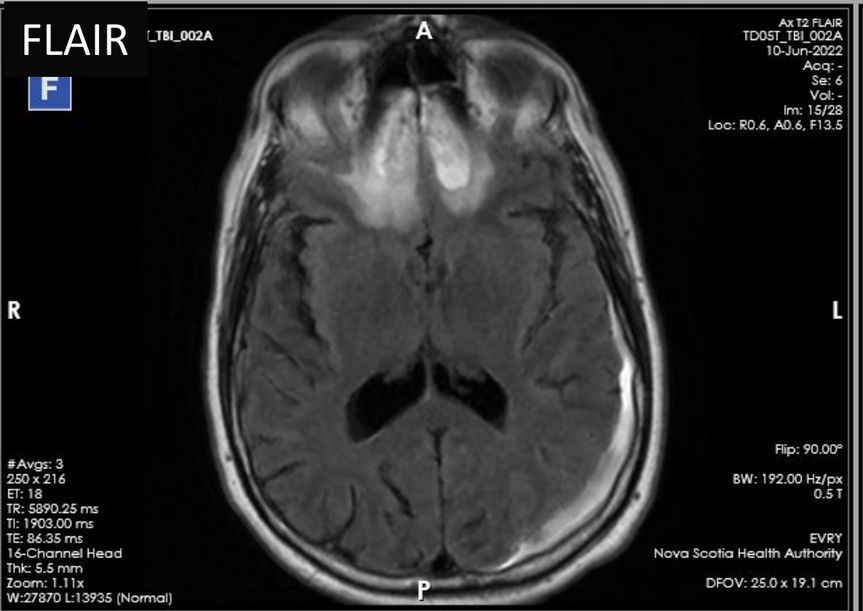
“Exploring the role of in-patient magnetic resonance imaging use among admitted ischemic stroke patients in improving patient outcomes and reducing healthcare resource utilization” Front. Neurol., 17 March 2024

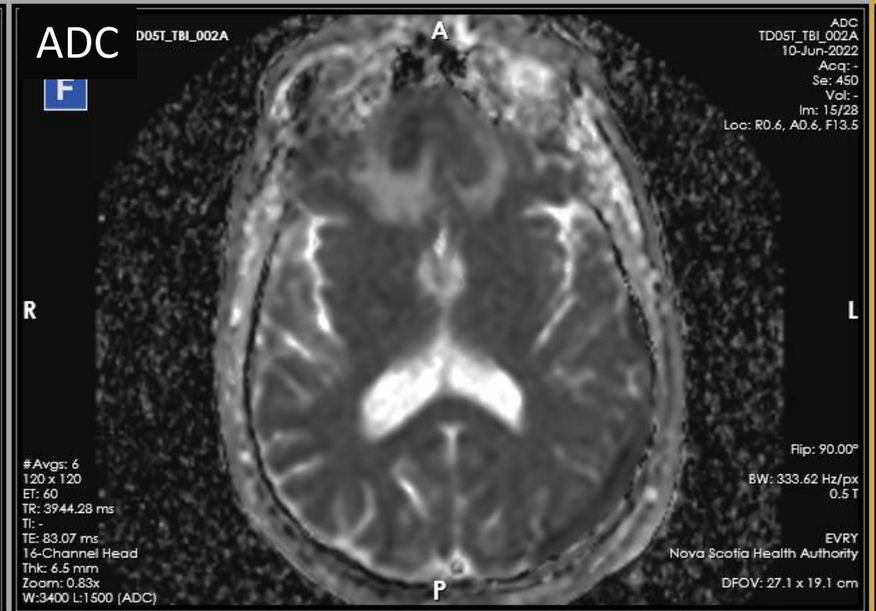
TBI Imaging: MRI in the ED

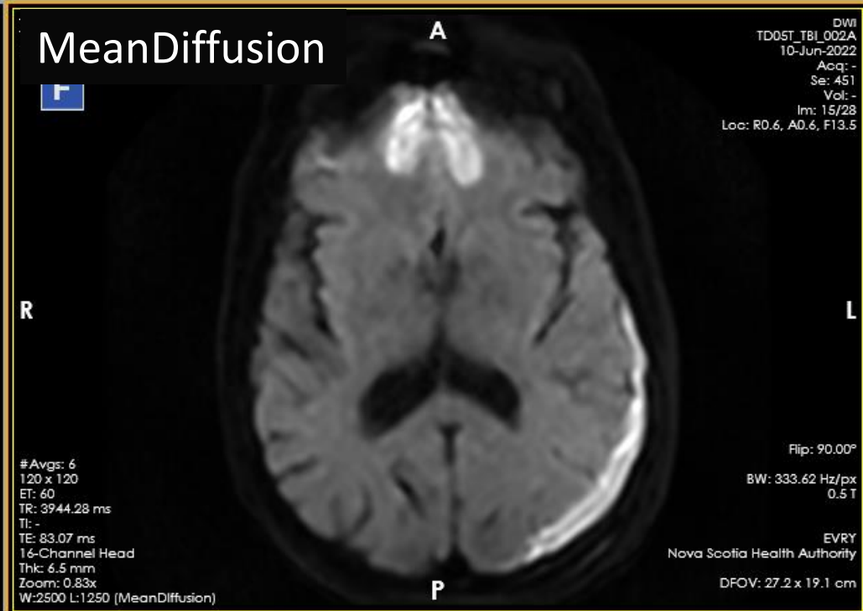




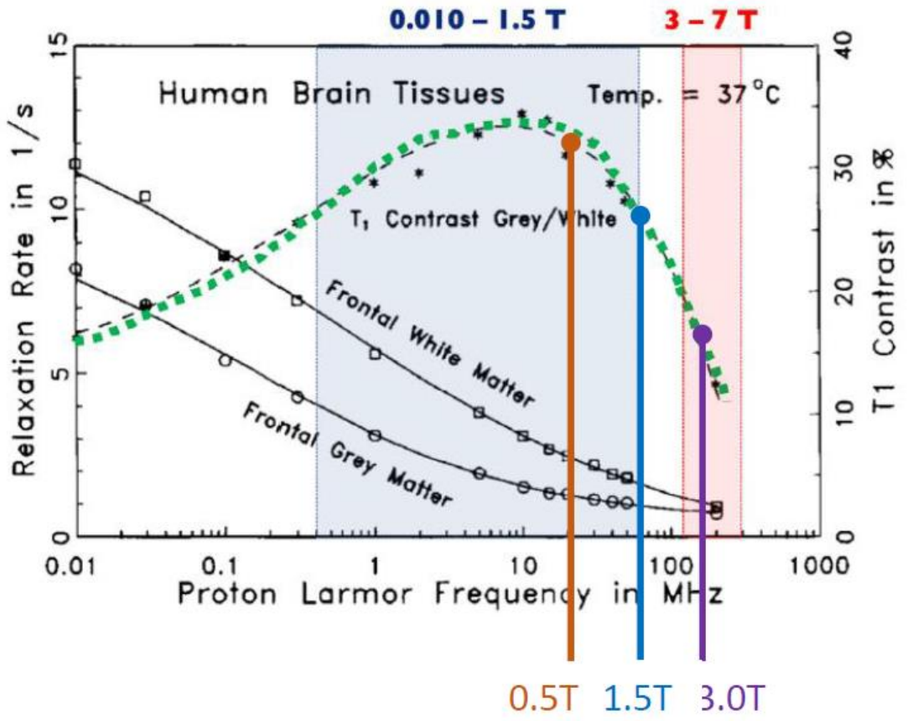






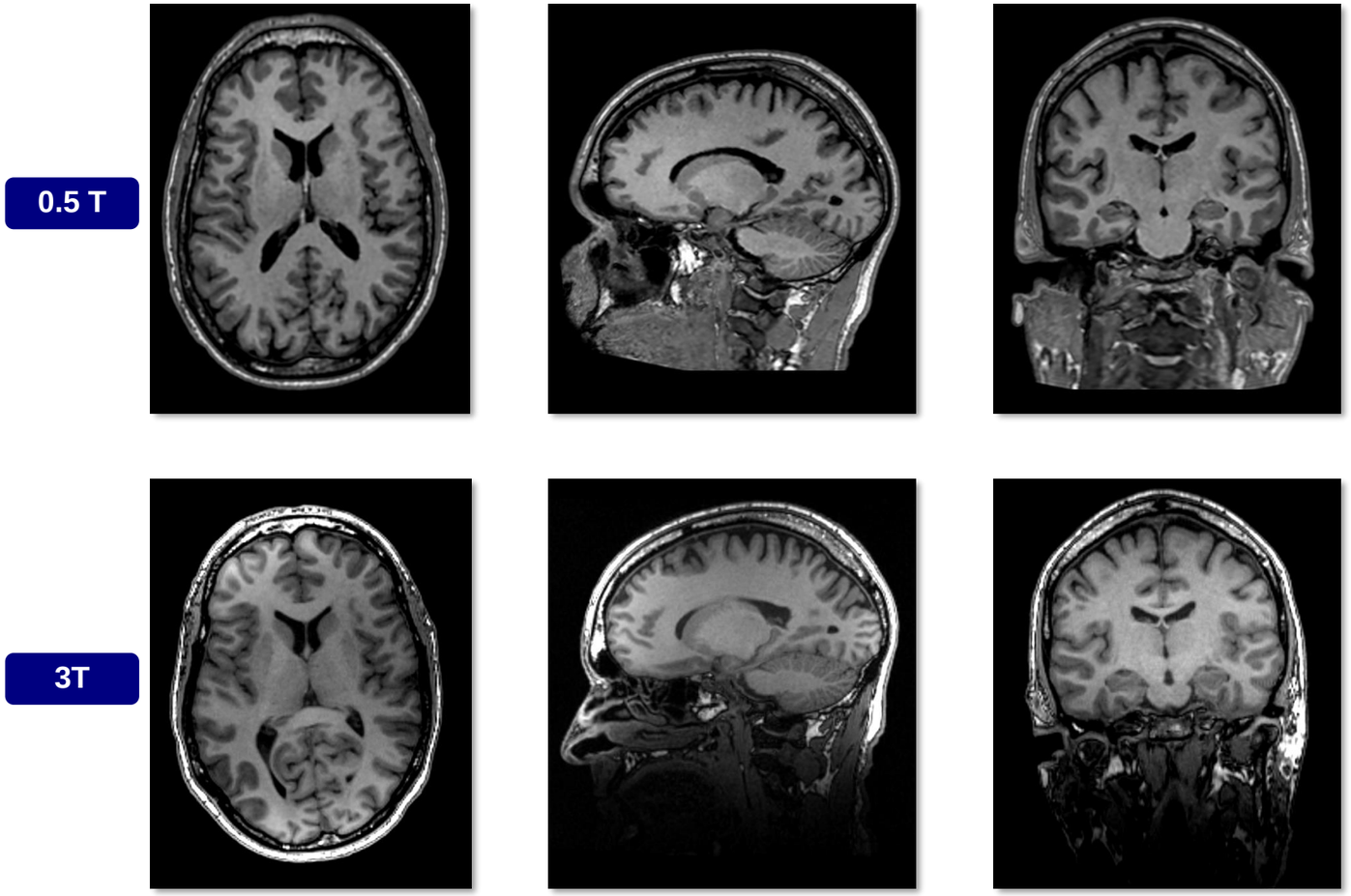


Synaptive 0.5T MRI: High Quality 3D T1 Imaging at 0.5T



WM / GM T1 contrast near optimum at 0.5T

Nuclear relaxation of human brain gray and white matter. Fischer HW, Rinck RA, Van Haverbeke Y, Muller RN. MRM 1990; 16: 317-334.



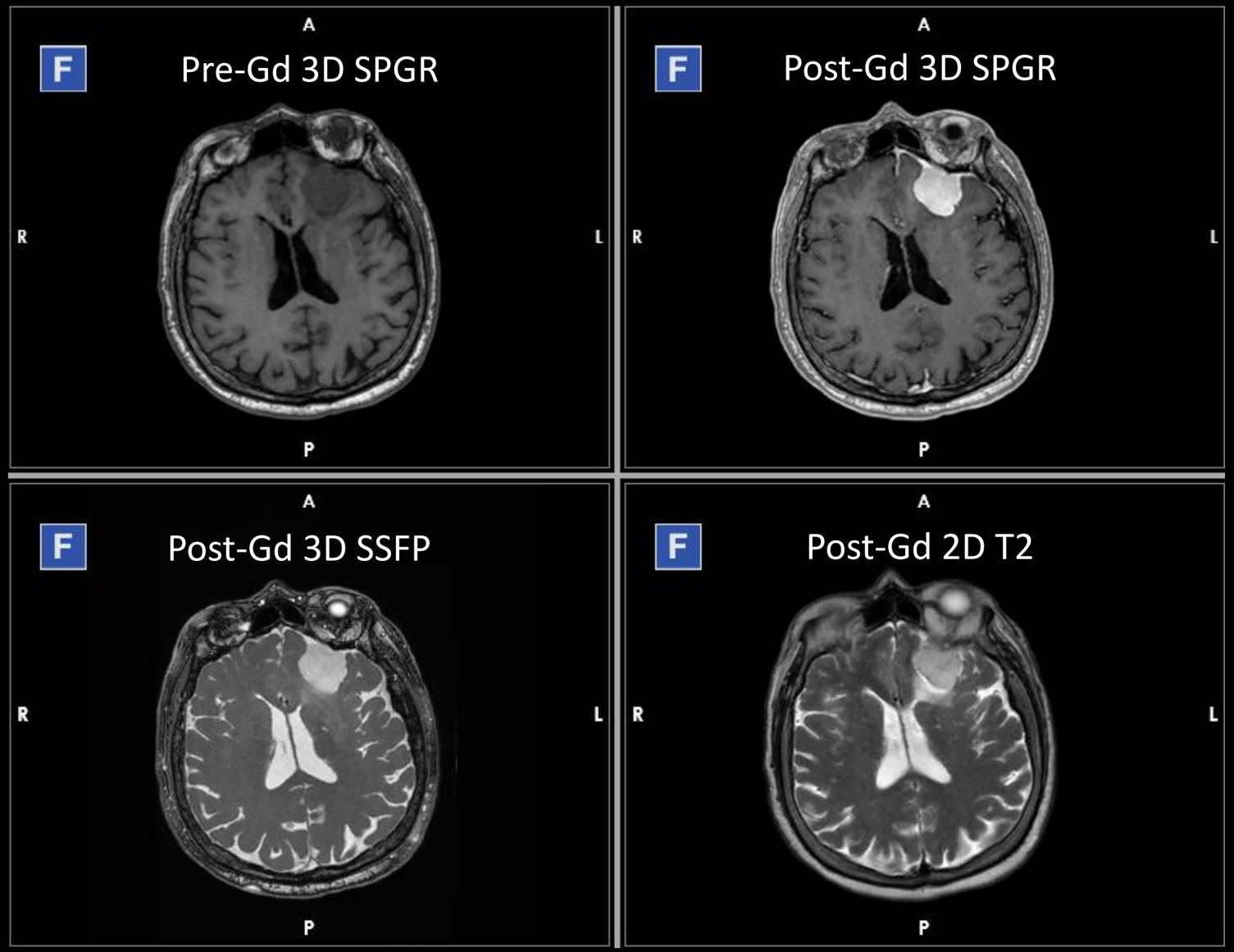
Exceptional hardware and system optimization of Synaptive MRI combined with the MRI fundamental of higher contrast at mid-field is leading to exceptional imaging quality for neuro applications.

Very strong IP position protecting these unique combination of imaging advantages.

Radiation Therapy and Synaptive MRI Combination

ZAP-X System on Left, Synaptive MRI on Right (Red window is MRI Room)

Surgical and Radiation Therapy for Tumor: Meningioma



Images courtesy of Hackensack Meridian Jersey Shore University Medical Center

Combination of high tissue contrast and visualization of MRI Gadolinium contrast agent provides ideal tumor contrast

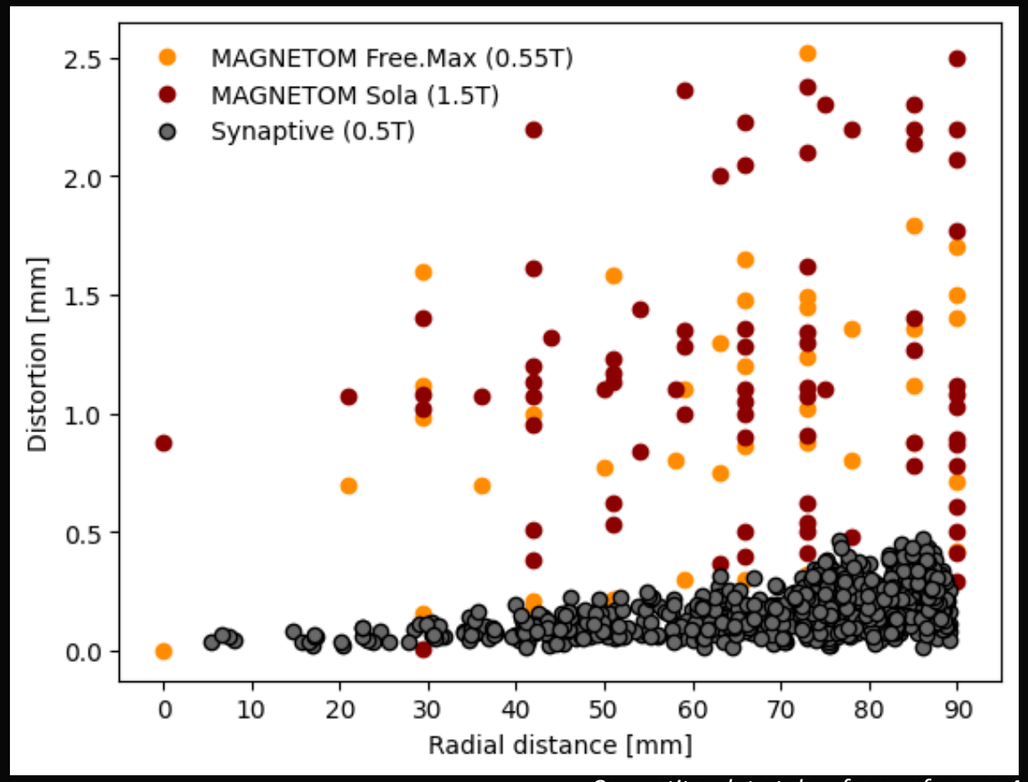
Under 1mm (mean) geometric accuracy in MRI scan versus **5mm on high-field systems**

Publications demonstrating improvements in **1) patient preference and comfort, 2) shorter time to treatment, 3) more accurate targeting and 4) ease of operation**

Structural (volumetric) imaging
geometric fidelity

- Geometric fidelity leads to more consistent structural measurements[1]
- Patient induced distortions are less due to less susceptibility effects at 0.5T[1]
- MRI can provide geometric accuracy of CT

System	Mean [mm]	Max [mm]
Siemens Free.Max 0.55T[4]	1.2	2.52
Siemens Sola 1.5T[4]	1.1	2.51
Siemens Symphony Syngo 1.5T[5]	0.56	1.37
Siemens Skyra 3.0T[6]	0.82	1.92
GE Optima MR450w 1.5T[6]	0.66	1.99
Philips Intera Achieva Nova Dual 1.5T[5]	0.47	1.19
Synaptive System 1	**0.156**	**0.34**
Synaptive System 2	**0.161**	**0.40**
Synaptive System 3	**0.160**	**0.44**
Synaptive System 4	**0.219**	**0.47**
Synaptive Average	**0.17 ± 0.03**	**0.41 ± 0.05**



Competitor data taken from reference 4.

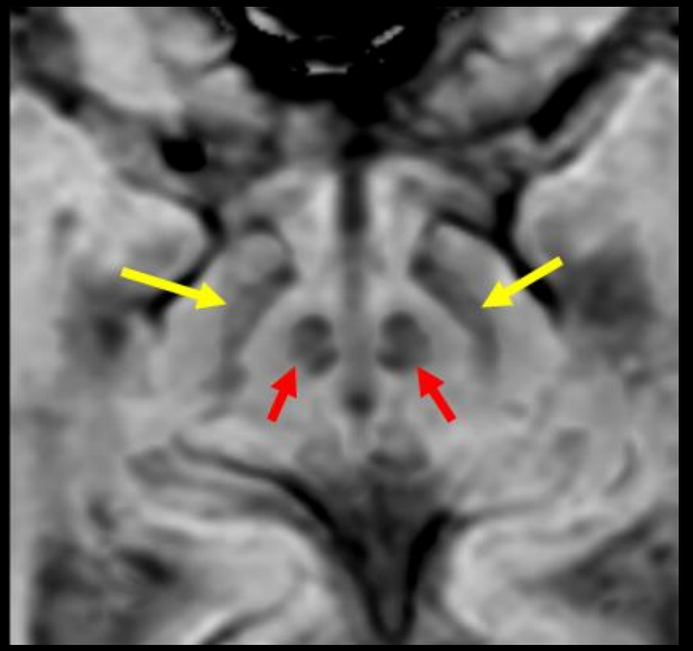
1. Nanayakkara, et al. Magn Reason Imaging 2022
2. Stanescu, et al. Medical Physics 2012
3. Wiens, et al. Medical Physics, in submission
4. Grigo, et al. Phys Imaging Radiat Oncol 2023.
5. Walker, et al. Australas Phys Eng Sci Med 2014.
6. Pappas, et al. Technology in Cancer Research & Treatment 2017

Visualization of Deep Brain Stimulation Targets at 0.5T

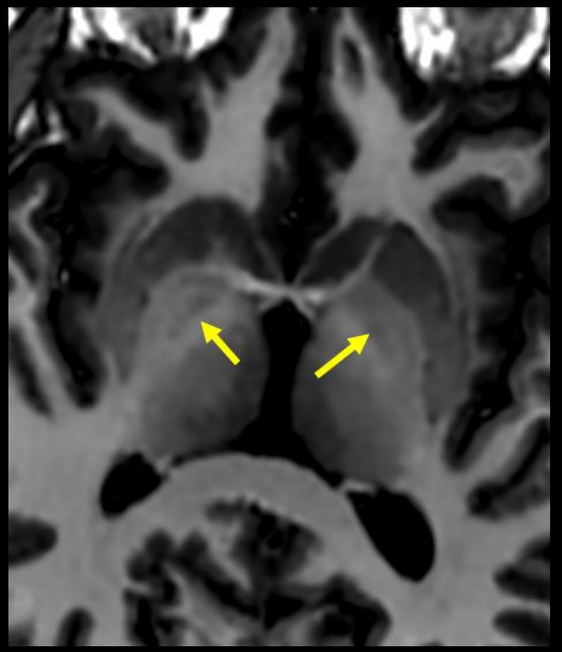
Device Imaging Work-flows often use X-Ray protocols

1) 3D SWI images show direct visualization of the subthalamic nuclei and surrounding iron-rich structures.

2) With the excellent gray/white matter contrast possible at mid-field, 3D T1-weighted imaging can directly visualize the globus pallidus interna.



1



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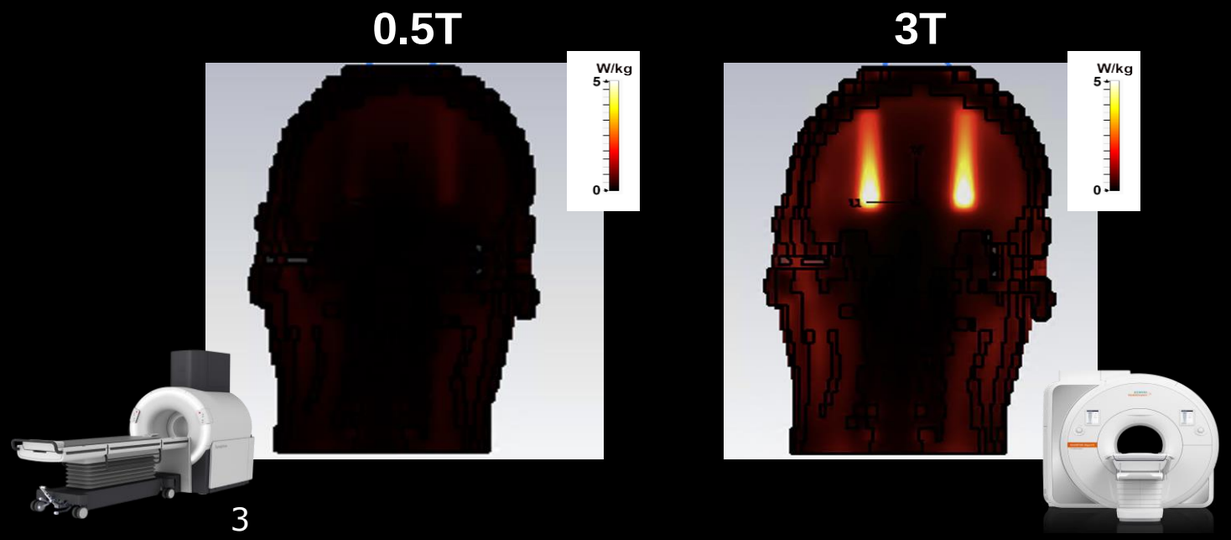


3

3) Imaging of brain and DBS probes after implantation is made extremely difficult due to heating of conductors in high field MRI systems (over 1.5T). The Synaptive MRI allows for imaging using all advanced sequences with electrodes implanted which has been thought impossible. CT can be eliminated at all stages of the work-flow.

MRI in Alzheimer’s Disease

Lilly's Kisunla™ (donanemab-azbt) Approved by the FDA for the Treatment of Early Symptomatic Alzheimer's Disease

July 2, 2024

Kisunla slowed cognitive and functional decline by up to 35% compared to placebo at 18 months in its pivotal Phase 3 study and reduced participants' risk of progressing to the next clinical stage of disease by up to 39%

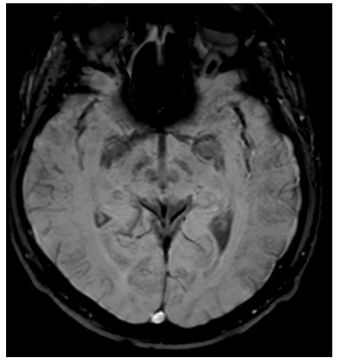
Download PDF

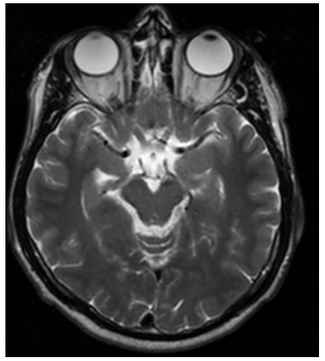
Kisunla is the first and only amyloid plaque-targeting therapy that used a limited-duration treatment regimen based on amyloid plaque removal; nearly half of study participants completed their course of treatment with Kisunla in 12 months

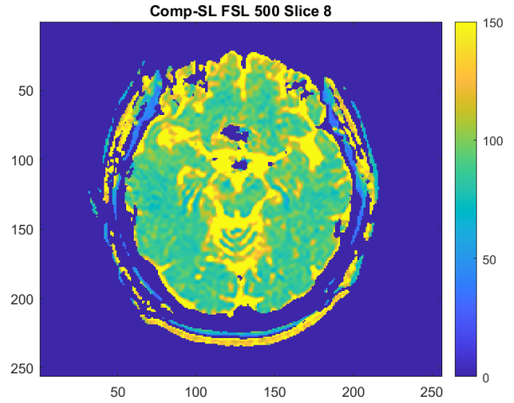
Once-monthly infusions of 30 minutes reduced amyloid plaques on average by 84% compared to the start of the study

INDIANAPOLIS, July 2, 2024 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) approved Kisunla™ (donanemab-azbt, 350 mg/20 mL once-monthly injection for IV infusion), Eli Lilly and Company's (NYSE: LLY) Alzheimer's treatment for adults with early symptomatic Alzheimer's disease (AD), which includes people with mild cognitive impairment (MCI) as well as people with the mild dementia stage of AD, with confirmed amyloid pathology.[1, 2] Once-monthly Kisunla is the first and only amyloid plaque-targeting therapy with evidence to support stopping therapy when amyloid plaques are removed, which can result in lower treatment costs and fewer infusions.[3-6]

"Kisunla demonstrated very meaningful results for people with early symptomatic Alzheimer's disease, who urgently need effective treatment options. We know these medicines have the greatest potential benefit when people are treated earlier in their disease, and we are working hard in partnership with others to improve detection and diagnosis," said Anne White, executive vice president and president of Lilly Neuroscience, Eli Lilly and Company. "Our deepest thanks to the patients and their loved ones for participating in our clinical programs and to Lilly scientists and collaborators persevering over decades of research. Each year, more and more people are at risk for this disease, and we are determined to make life better for them."





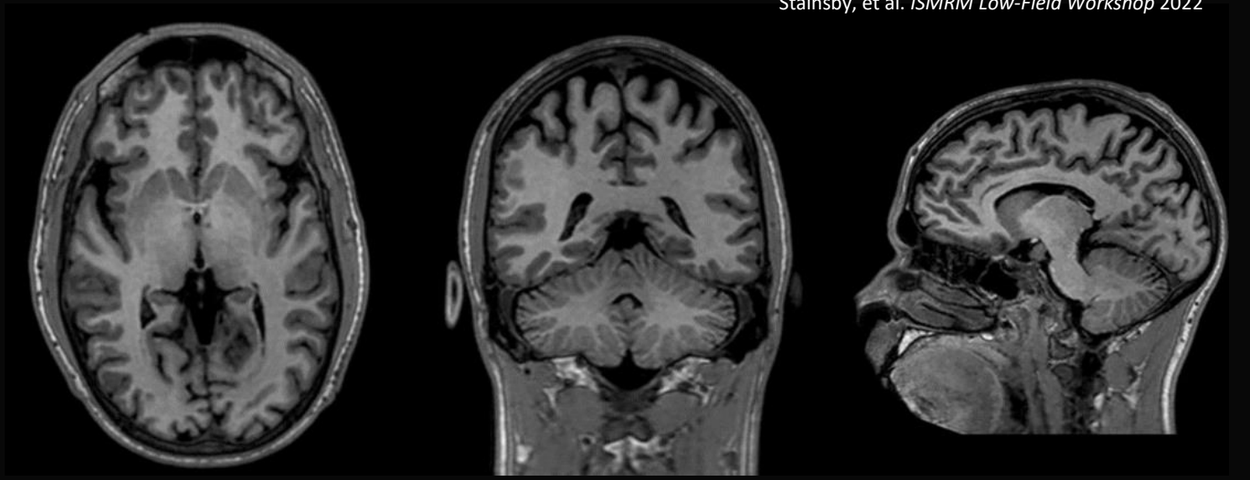


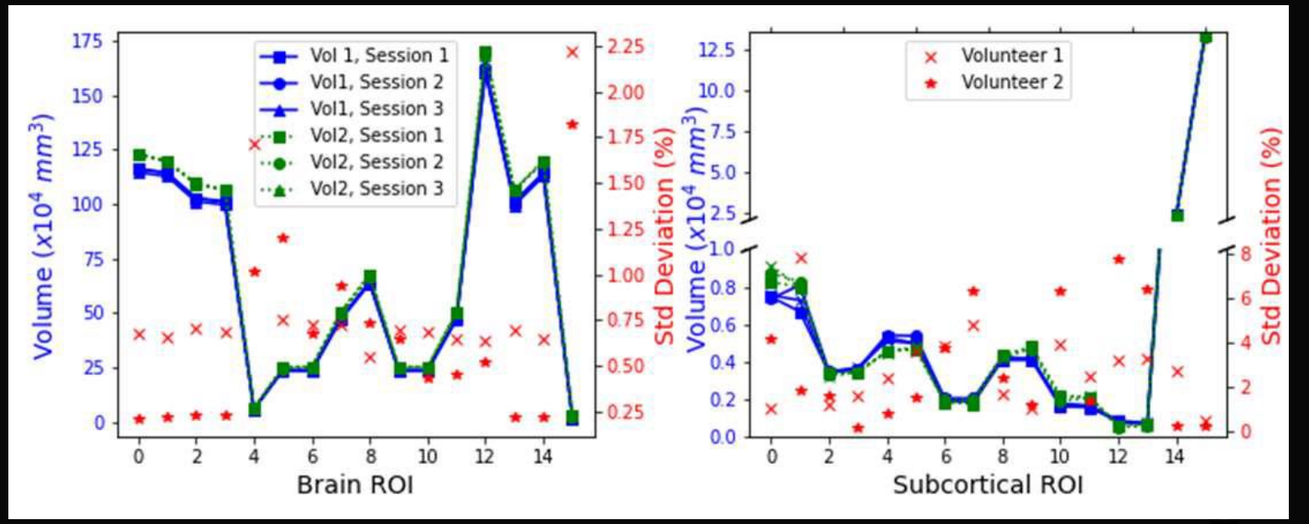
- Demand for MRI accelerating due to new drug infusions requiring 5 MRI scans yearly for safety monitoring (ARIA = Amyloid Related Imaging Abnormalities)
- Synaptive MRI ideal for these scans with venue flexibility and ideal patient requirement fit (accessible, low-noise, low-anxiety imaging)
- MRI as a replacement for PET scans with serial imaging capability

Structural (volumetric) imaging
consistency is vital

- Measured brain volumes are influenced by many things
  - e.g., coil shading, patient induced distortions, system-to-system hardware variations
- Across brain regions at 3T intra-site and intra-vendor average variability were reported to be 11.36% and 14.69% respectively[1]
- Preliminary intra-site data taken with Synaptive MR averaged 0.8% and 3.5% variability over larger regions and subcortical volumes respectively[2]
- This enables more consistent inputs into automated analysis platforms

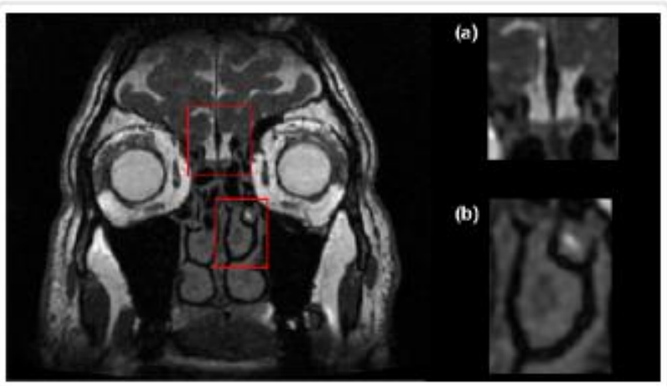
Stainsby, et al. *ISMRM Low-Field Workshop* 2022





1. Bosco, et al. Phys Med 2023; doi:10.1016/j.ejmp.2023.102577
2. Stainsby, et al. *ISMRM Low-Field Workshop* 2022

Sinus/Ear Imaging



A demonstration of the high isotropic resolution achieved in the coronal view by the axial bSSFP acquisition. Visualization of the cribriform plate (top box and image (a)) is important when identifying critical variants. The left middle turbinate of the ostiomeatal complex (bottom box and image (b)) is examined for anatomical variants, opacification of drainage pathways, and mucosal thickening.

Can a sub 2-minute MRI exam compete with CT for imaging sinus anatomy?

Sarah Reeve[1,2], Mark Parker[2,3], James Rioux[1,2,4], Elena Adela Cora[4,5], Chris Bowen[1,2,4], Steven Beyea[1,2,4,6], and David Volders[4,5]

[1]Physics and Atmospheric Science, Dalhousie University, Halifax, NS, Canada, [2]Biomedical Translational Imaging Centre, QEII Health Sciences Centre, Halifax, NS, Canada, [3]Medicine, Dalhousie University, Halifax, NS, Canada, [4]Diagnostic Radiology, Dalhousie University, Halifax, NS, Canada, [5]Diagnostic Imaging, Nova Scotia Health, Halifax, NS, Canada, [6]School of Biomedical Engineering, Dalhousie University, Halifax, NS, Canada

The protocol included an axial bSSFP (T2/T1 weight) sequence acquired at 0.5-T with gradients operated at a maximum strength of 50 mT/m and a slew rate of 200 T/m/s. Sequence parameters selected were 18cm FOV, 226x226 acquisition matrix, NEX=1, RBW=150kHz, TR/TE = 3.5ms/1.6ms, flip-angle=30°. Images were acquired with isotropic resolution of 0.8mm and interpolated onto a 0.4mm grid. These parameters resulted in a scan time of 1min52s without reaching specific absorption rate limits.

Abstract Title: Leveraging low field with high performance gradients enables MR imaging of the internal auditory canal and paranasal sinuses

Author List: Sarah Reeve, Mark Parker, Chris Bowen, James Rioux, David Morris, Steven Beyea, David Volders

Results:

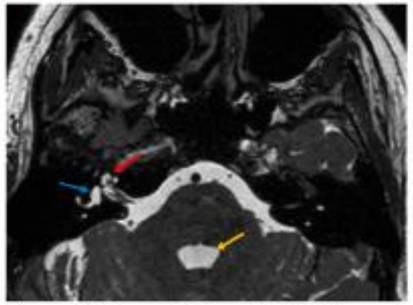


Figure 1: Representative axial bSSFP acquisition from the IAC protocol. ROIs for the right cochlea (red) vestibulum (blue) and 4th ventricle (yellow) were drawn in the axial plane.

Structure	Mean SNR	95% C.I.
4th Ventricle	189.77	(158.91, 220.64)
White Matter	39.92	(33.73, 46.12)
Left SSC	128.97	(108.77, 149.16)
Left Vestibule	163.36	(138.69, 188.02)
Left Cochlea	140.53	(120.06, 161.00)
Left Nerve Region	142.71	(121.67, 163.76)
Right SSC	129.03	(109.15, 148.92)
Right Vestibule	163.68	(137.08, 190.29)
Right Cochlea	136.76	(117.86, 155.66)
Right Nerve Region	138.36	(116.42, 160.30)

Table 1: Mean SNR and associated 95% confidence intervals across subjects for structures examined in the IAC acquisitions. SSC refers to the superior semicircular canal, and "nerve region" refers to the high-intensity region surrounding the facial, cochlear, and vestibular nerves. All ROIs were drawn in the plane where the structure was best visualized.

- High-resolution and rapid imaging has been difficult for MRI
- 0.5T has demonstrated 0.4mm iso-tropic scanning in a 2 min protocol
- With AI accelerated imaging, this could be done in 15 seconds