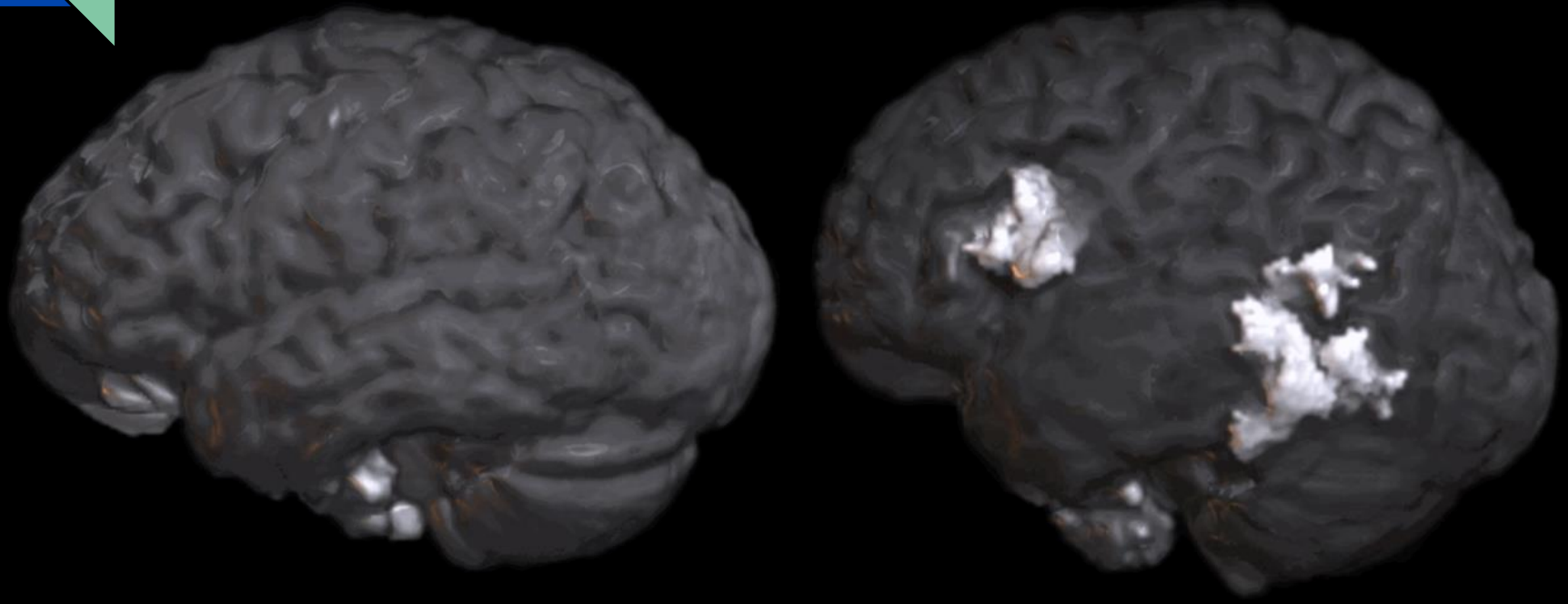
Clinical Evaluation of Three MR Tractography Software

Sam Butler, University Hospitals of North Midlands NHS Trust

Introduction

- Motivation
- Tractography Recap
- Part 1: Acquisition
- Part 2: Processing
- Part 3: Assessment of three processing software
  - Syngo.Via (Siemens Healthineers)
  - Brainance MD (Advantis Medical Imaging)
  - MRTrix (J.-D. Tournier et al., 2019)

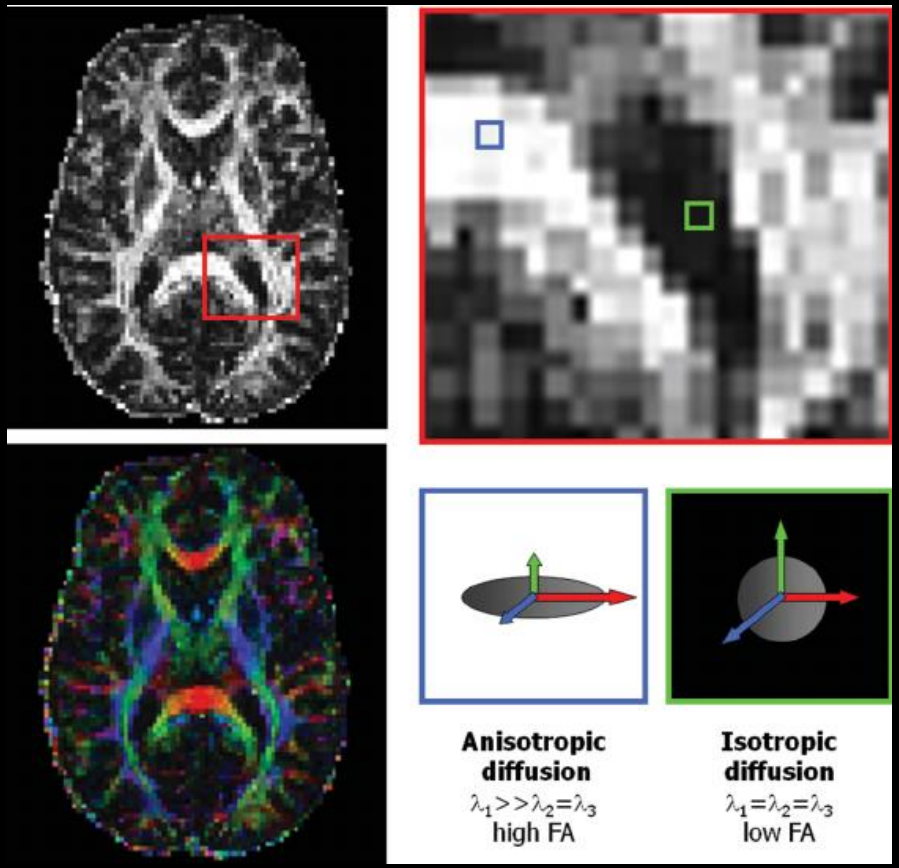
Motivation



2020

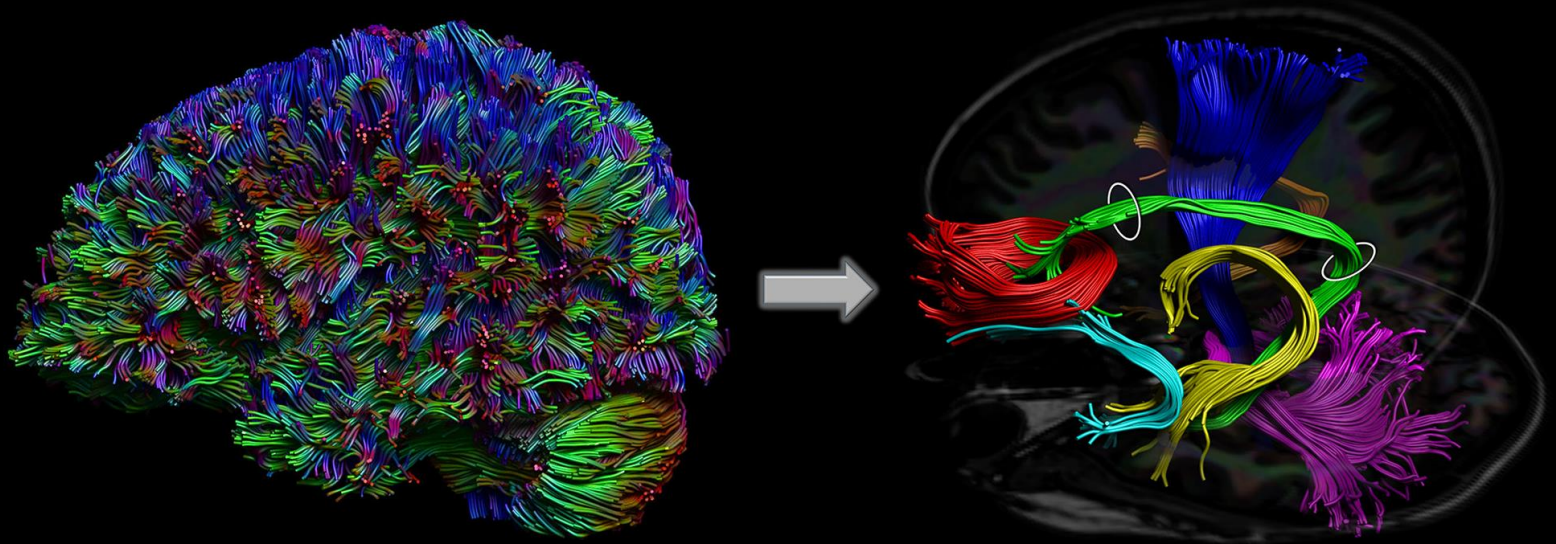
2022

Tractography Recap



(Geva et al., 2011)

Tractography Recap

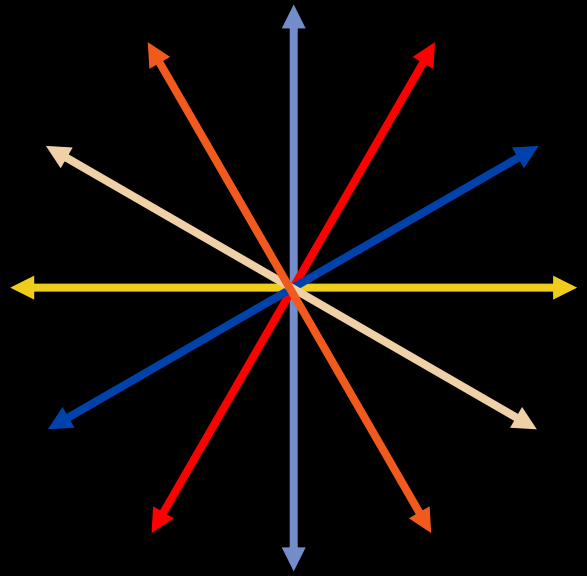


(Jeurissen et al., 2017)

Part 1: Acquisition

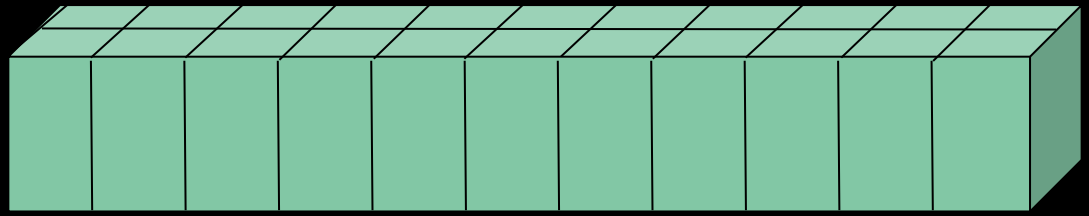
Problems

- Number of directions



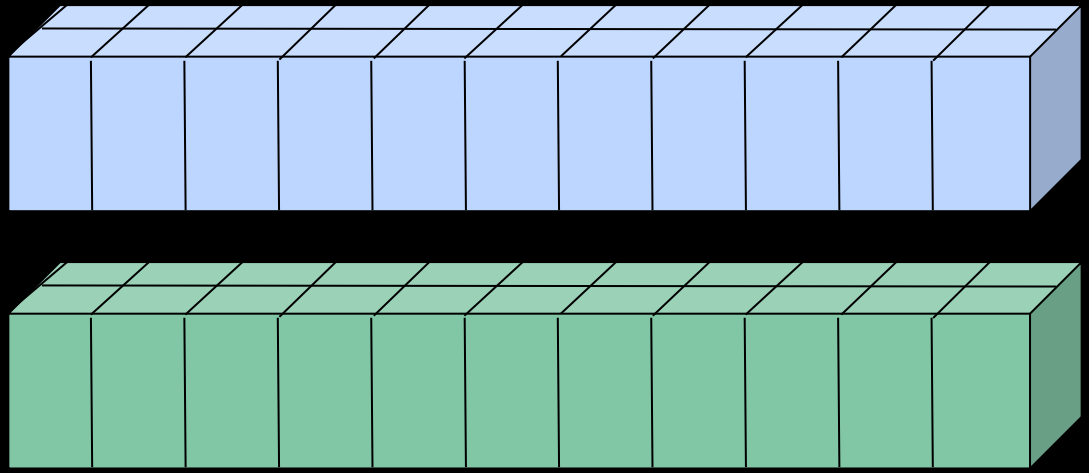
Problems

- Number of directions
- Voxel size



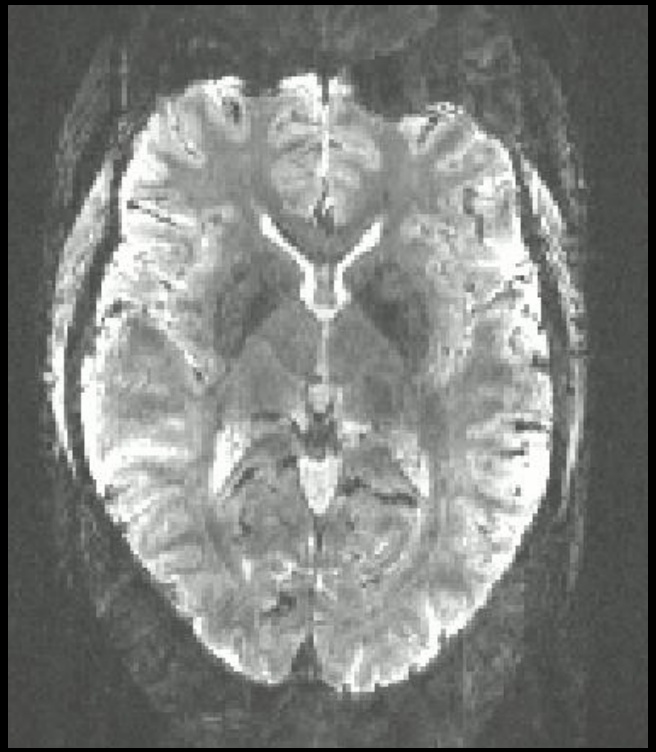
Problems

- Number of directions
- Voxel size
- Slice gap



Problems

- Number of directions
- Voxel size
- Slice gap
- Distortions

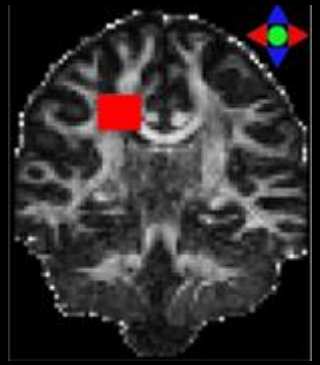


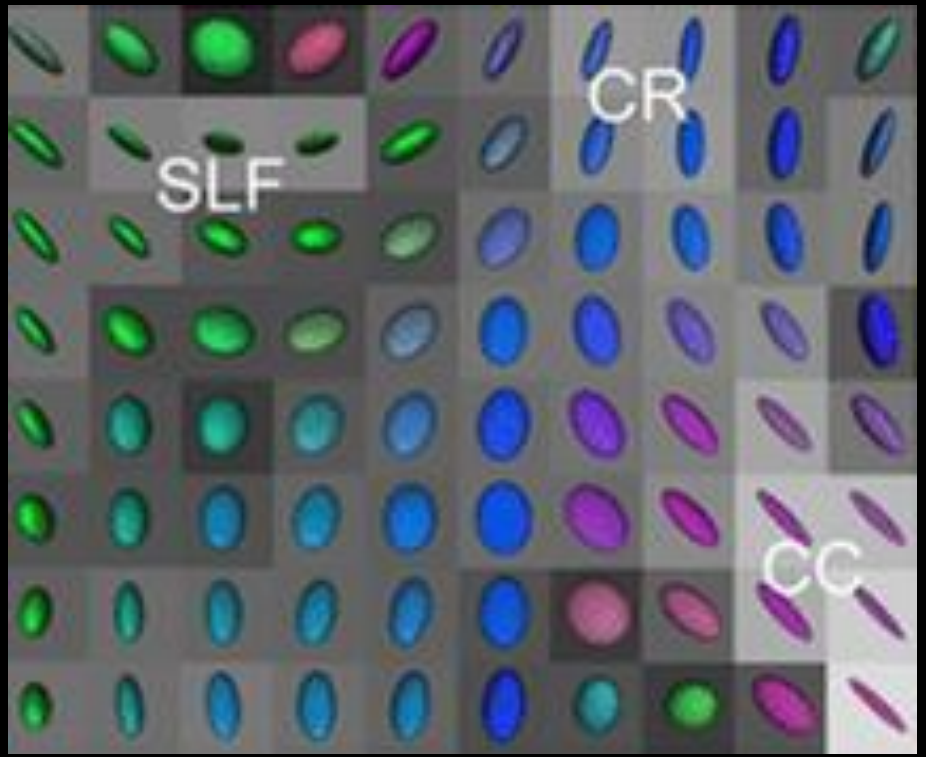
Solution: Optimised Sequence

- 30 directions
  - (more is preferable, but limited by gradients & acquisition time)
- b0, b1000 and b1500
  - (b>1500 preferable, but limited by gradients & acquisition time)
- 2.5mm isotropic
- No slice gap
- SMS enabled (p2, s2)
- AP and PA images acquired
- Partial Fourier

Part 2: Processing

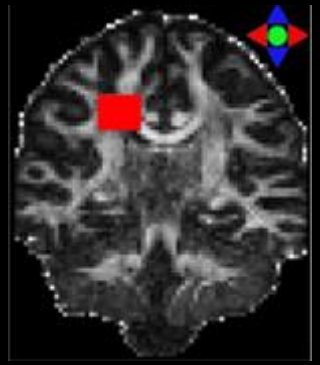
Processing: Tensors

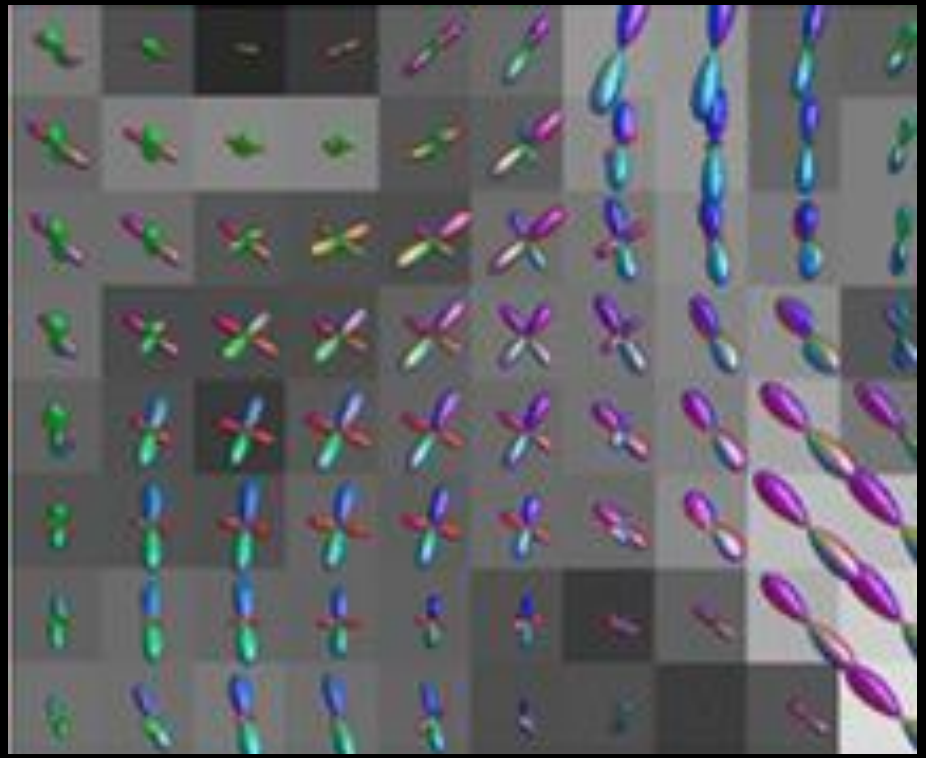




(Tian et al., 2022)

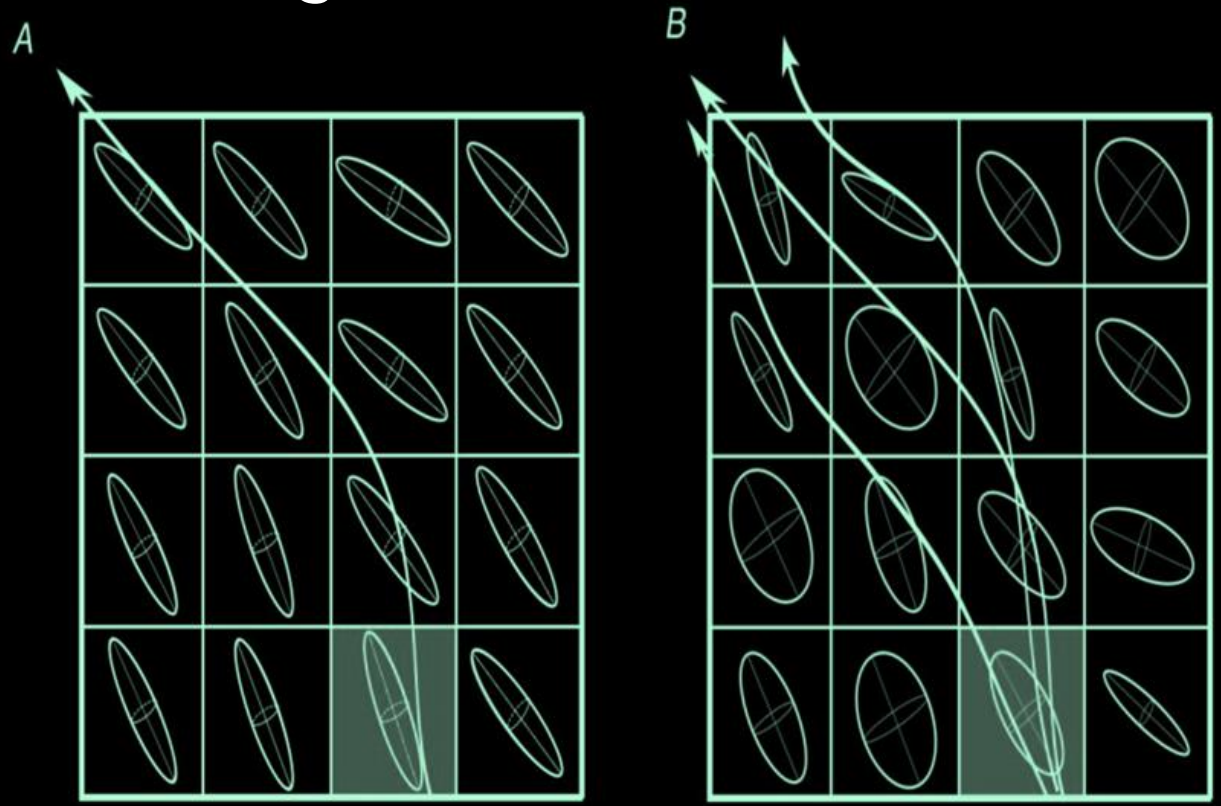
Processing: Orientation Density Function





(Tian et al., 2022)

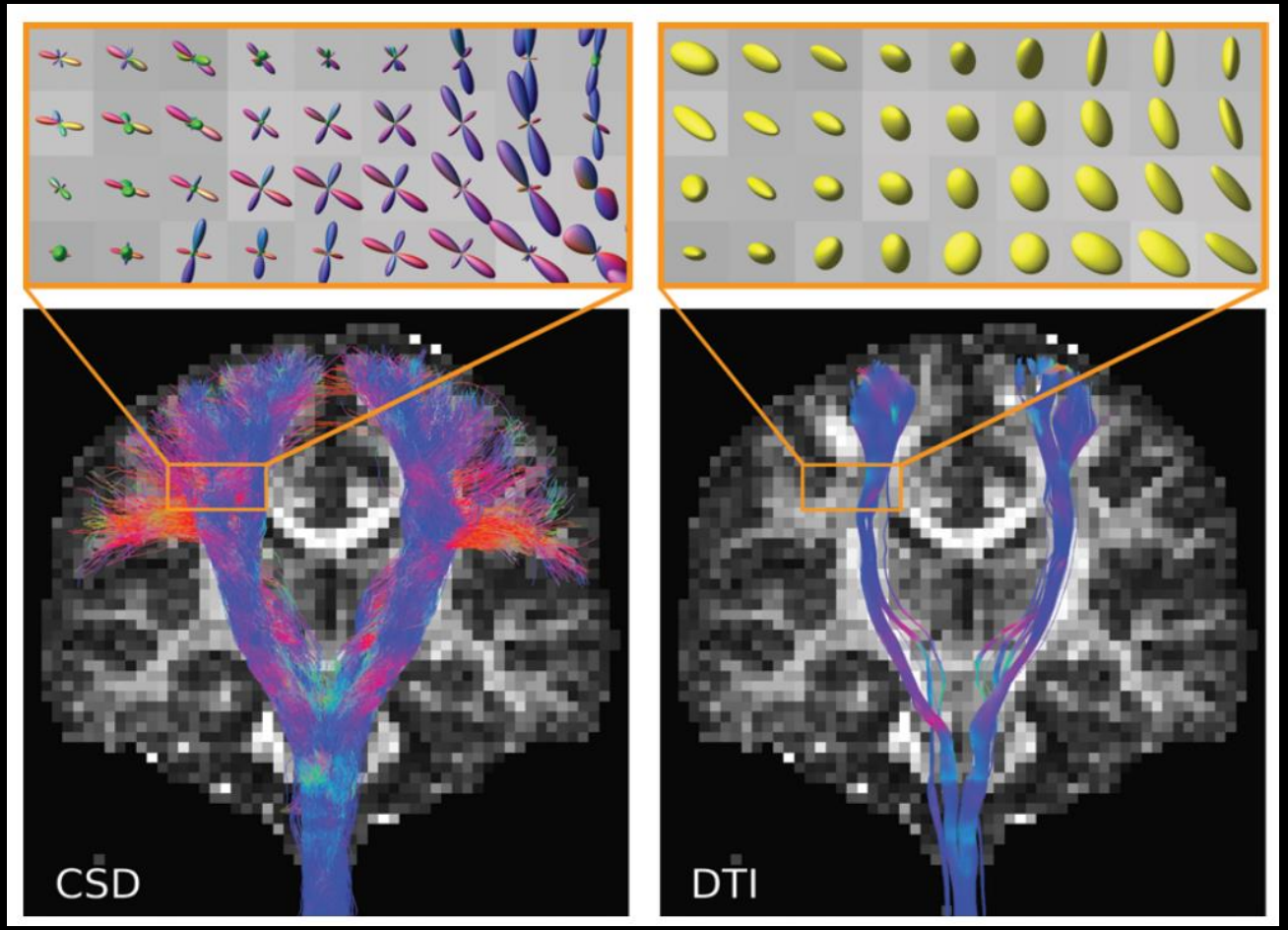
Processing



Deterministic

Probabilistic

(Rodrigues et al., 2018)



(Farquharson, S. *et al.*, 2013)

Processing: (Some) Other Considerations

- Seed ROIs
- Include/Exclude ROIs
- Step size
- Stopping criteria
    - e.g. maximum curvature, maximum length, tracking mask

Part 3: Clinical Evaluation

Clinical Comparison

Three software:

- Syngo.Via
  - Deterministic DTI
- Brainance MD
  - “Mostly based on the principles of the deterministic logic”
- MRTrix
  - Probabilistic MSMT CSD
  - AP + PA distortion correction

Reconstructed two tracts for 9 brain tumour patients

- Corticospinal Tract (CST)
- Arcuate Fasciculus (AF)

Clinical Comparison

Assessed by two consultant neuroradiologists on:

1. Chosen tract generation (scored 1 – 5)
   Scored 1 (no tract generation) to 5 (complete tract generation)

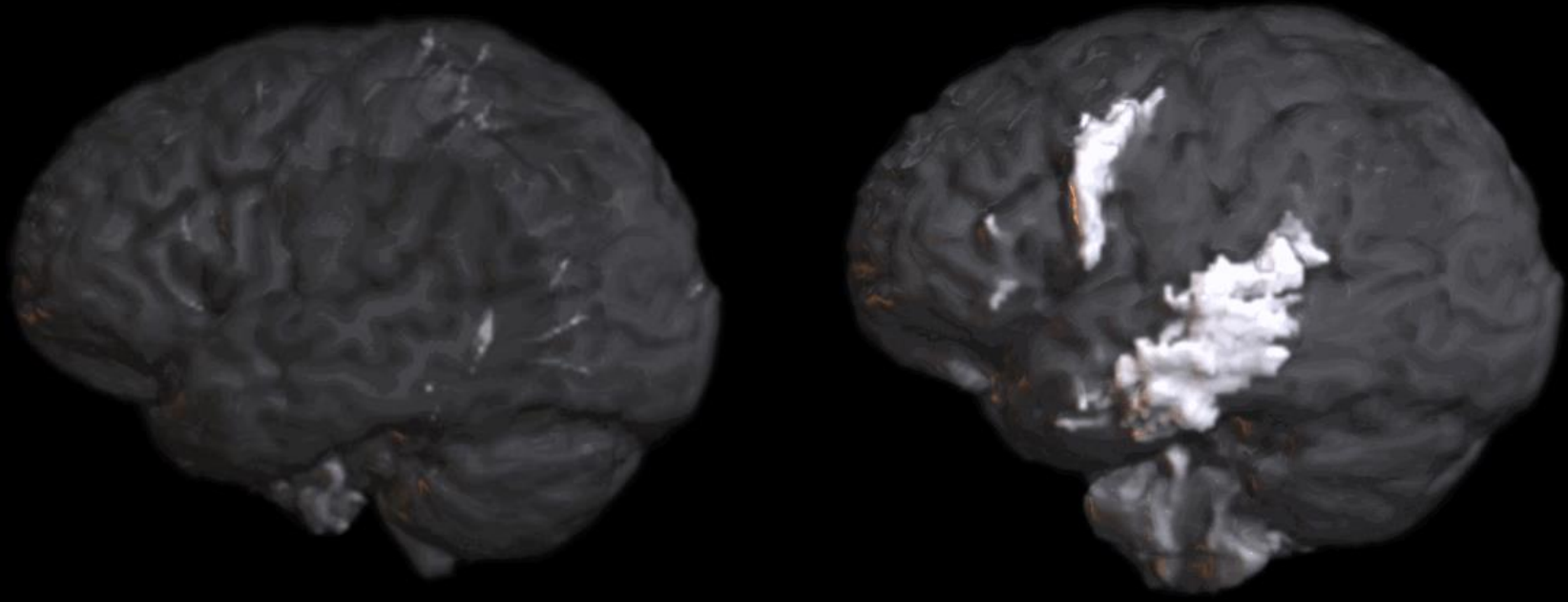
2. Anatomical Accuracy
   Scored 1 (incorrect anatomical location) to 5 (correct anatomical location)

3. Spurious tracts
   Scored 1 (excessive spurious tracts) to 3 (no spurious tracts)

Clinical Comparison

	Tract Generation		Anatomical Accuracy		Spurious Tracts	
	AF	CST	AF	CST	AF	CST
SyngoVia	2.9 ± 0.9	3.2 ± 1.0	3.0 ± 1.7	4.1 ± 1.1	1.8 ± 0.6	2.3 ± 0.7
Brainance MD	3.8 ± 1.1	4.4 ± 0.5	3.6 ± 1.6	4.6 ± 0.7	2.7 ± 0.4	2.7 ± 0.5
MRTrix	5.0 ± 0.0	5.0 ± 0.0	4.9 ± 0.3	5.0 ± 0.0	3.0 ± 0.0	3.0 ± 0.0

Clinical Comparison: Case Study



Brainance MD

MRTrix

Limitations

- Only assessing two tracts
- Cost effectiveness not considered
- No robust comparison of crossing/kissing fibres
- No account for other features
- No assessment of sensitivity and specificity
- Other available CE marked software

Recommendations

- Talk to apps for sequence optimisation
- Talk to other centres!
- What is important for your centre?
  - Talk to radiologists
  - Talk to surgeons
- MRTrix is free, give it a go ☺
- Keep an eye out for UKCA marked software that meets your “must haves”

Summary

- Lots to think about!
- “Out of the box” acquisition not adequate for accurate reconstruction.
- MSMT CSD technique gave best results
- MRTrix > Brainance MD >>> Syngo.Via
- Share knowledge to help everyone improve

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J.-D. Tournier, R. E. Smith, D. Raffelt, R. Tabbara, T. Dhollander, M. Pietsch, D. Christiaens, B. Jeurissen, C.-H. Yeh, and A. Connelly. *MRtrix3*: A fast, flexible and open software framework for medical image processing and visualisation. NeuroImage, 202 (2019), pp. 116–37.

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uclh

Accurate localization of tracts during brain tumour resection in an interventional MRI suite

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IPEM
Institute of Physics and Engineering in Medicine

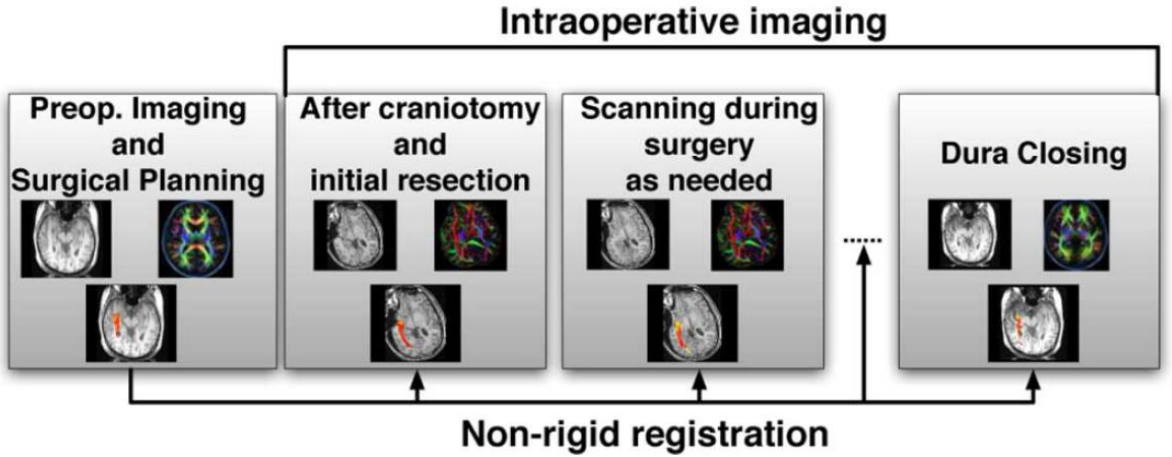
Background

- Aim of surgery: maximum resection, minimum deficit
- Dissecting iop-tract very hard:
  - Image quality (coil, open craniotomy…)
  - Limited time for data acquisition and analysis
  - Anatomy distorted
  - CSD only available since Feb 2022 on Medtronic Stealth

882 IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 31, NO. 4, APRIL 2012

Accurate Localization of Optic Radiation During Neurosurgery in an Interventional MRI Suite

Pankaj Daga*, Gavin Winston, Marc Modat, Mark White, Laura Mancini, M. Jorge Cardoso, Mark Symms, Jason Stretton, Andrew W. McEvoy, John Thornton, Caroline Micallef, Tarek Yousry, David J. Hawkes, John S Duncan, and Sebastien Ourselin



anterior temporal lobe resection for treating refractory focal epilepsy

T1 + FA

Methodology

Image registration:

- Bivariate normalised mutual information (NMI)
- Unified (T1+FA) similarity measure
- Modified version of the free form deformation algorithm

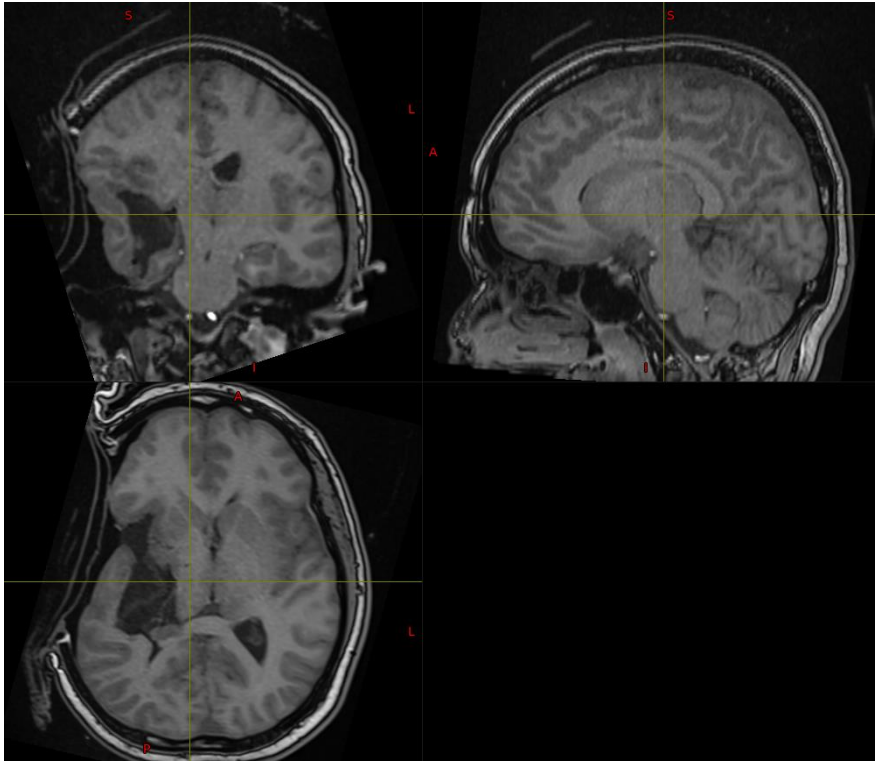
Patients

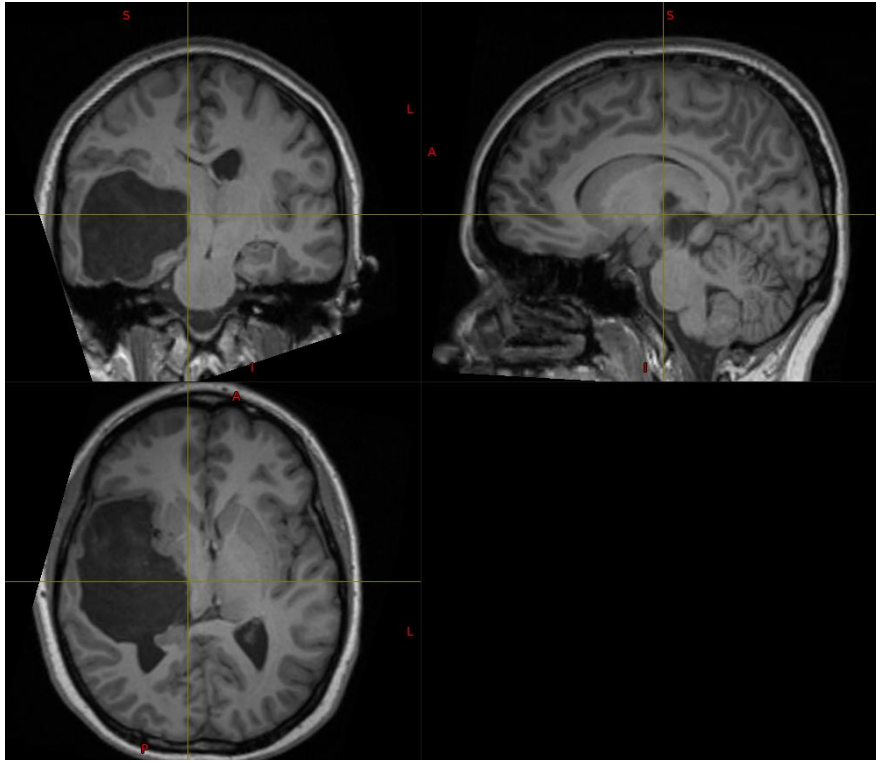
Subject	Tumour Location	Tracts Dissected	Pre-op DWI	Intra-op DWI
1	R Motor Strip	CST Hand, Foot, AF	64 dir, b 1000	30 dir, b 1000
2	Left Insular	CST Hand, AF, OR	64 dir, b 1000	3 x 12 dir, b 1000
3	R Temporal	CST Hand, AF, OR	64 dir, b 1000	3 x 12 dir, b 1000
4	Right Frontal	AF	64 dir, b 1000	3 x 12 dir, b 1000
5	R Anterior Temporal	OR	64 dir, b 1000	30 dir, b 1000
6	R Frontal Cyngulum	AF	60/32/12 dir, b 2000/700/300	64 dir, b 1000
7	L Insula	CST Hand, AF, OR	60/32/12 dir, b 2000/700/300	64 dir, b 1000
8	R Frontal	AF	60/32/12 dir, b 2000/700/300	64 dir, b 1000
9	R Temporal	CST Hand, AF, OR	60/32/12 dir, b 2000/700/300	64 dir, b 1000
10	R Parietal	CST Hand, AF, OR	60 dir, b 1400	64 dir, b 1000
11	L Frontal	CST Hand, AF	60/32/12 dir, b 2000/700/300	64 dir, b 1000
12	R SFG	CST Hand, AF	60/32/12 dir, b 2000/700/300	64 dir, b 1000
13	L Anterior Temporal	OR	60 dir, b 1400	64 dir, b 1000
14	R Fusiform Gyrus	AF, OR	60 dir, b 1400	64 dir, b 1000
15	R Parietal	CST Hand, Foot, OR	60 dir, b 1400	64 dir, b 1000

Tracts

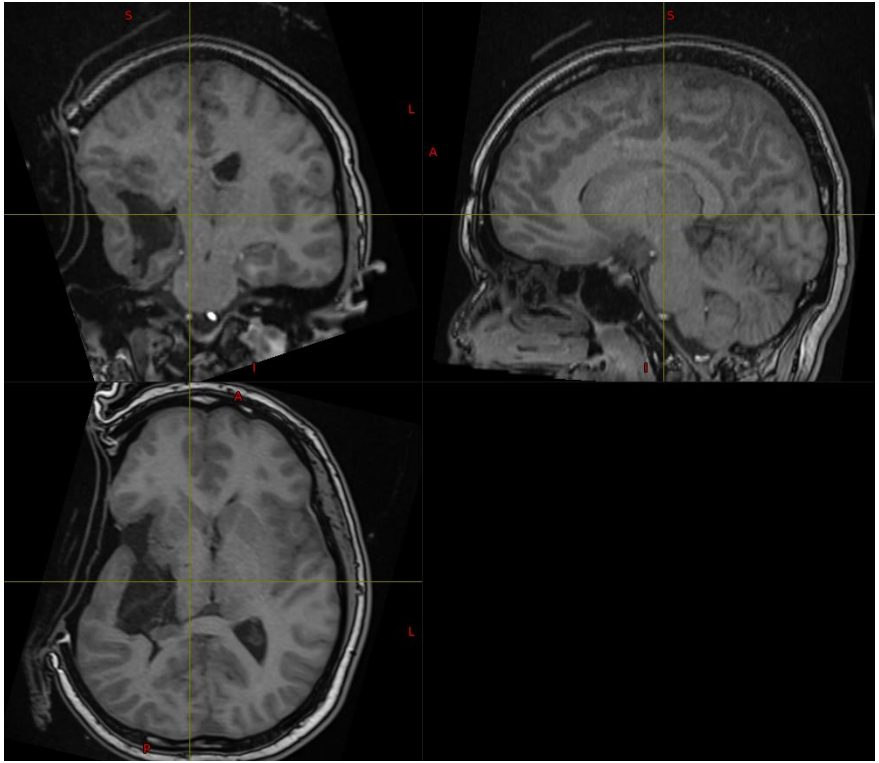
- Intra-op tracts as "gold standard"
- Pre-op tracts to intra-op space with non-rigid registration (NRR)
- Cannot be done with current commercial neuro-navigation systems
  - assume rigid relationship between pre- and intra-op images
- NRR integrates T1 + FA
- Time required < 5 min
  - excluding pre-processing of intra-op data

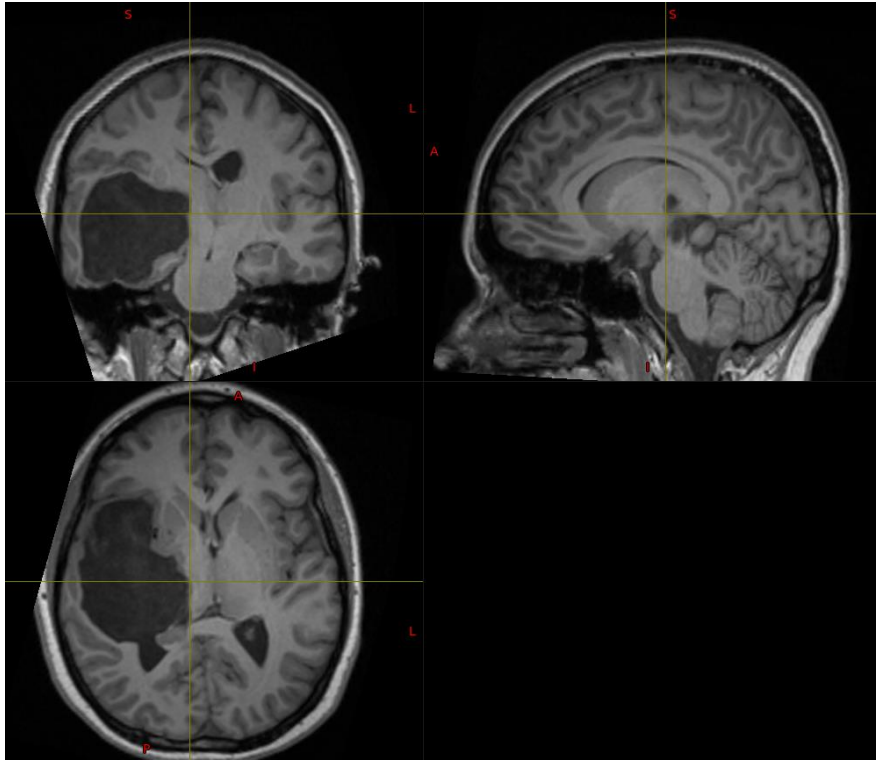
T1 RIGID



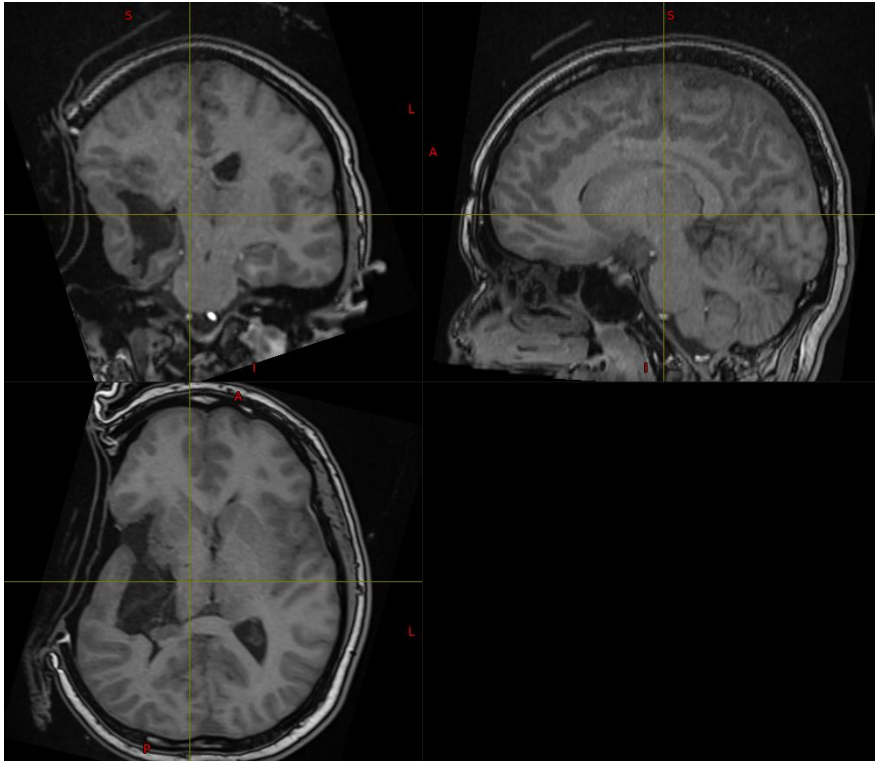


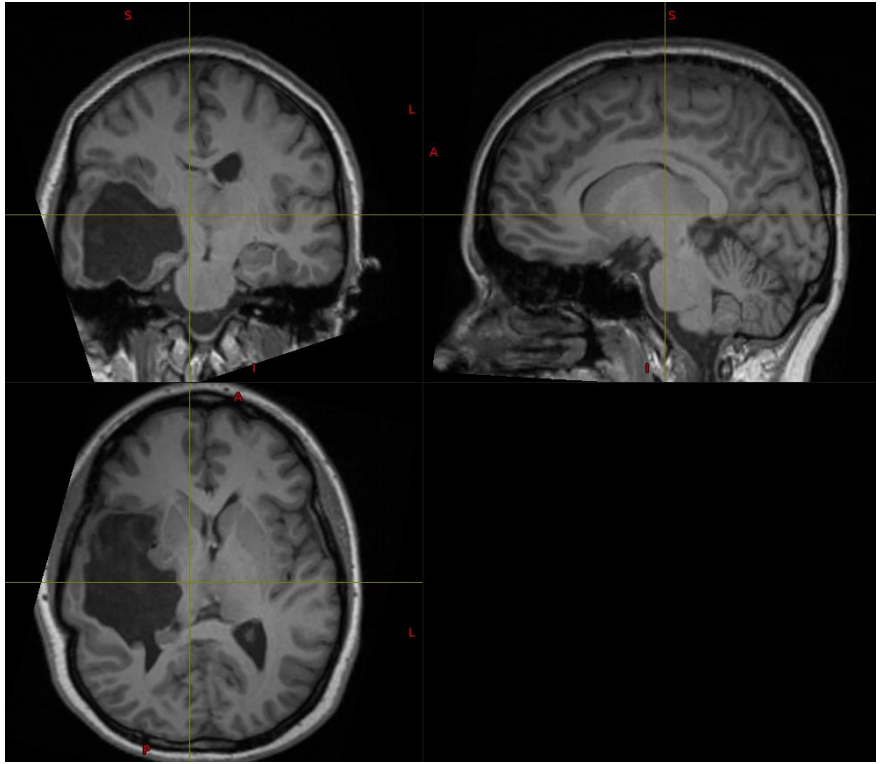
T1 AFFINE



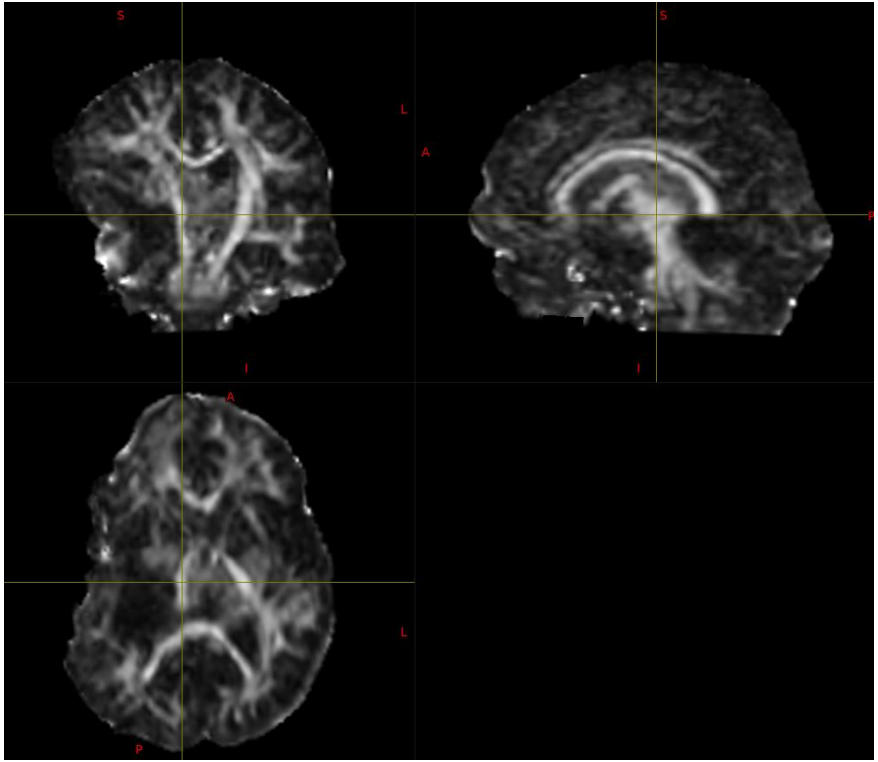


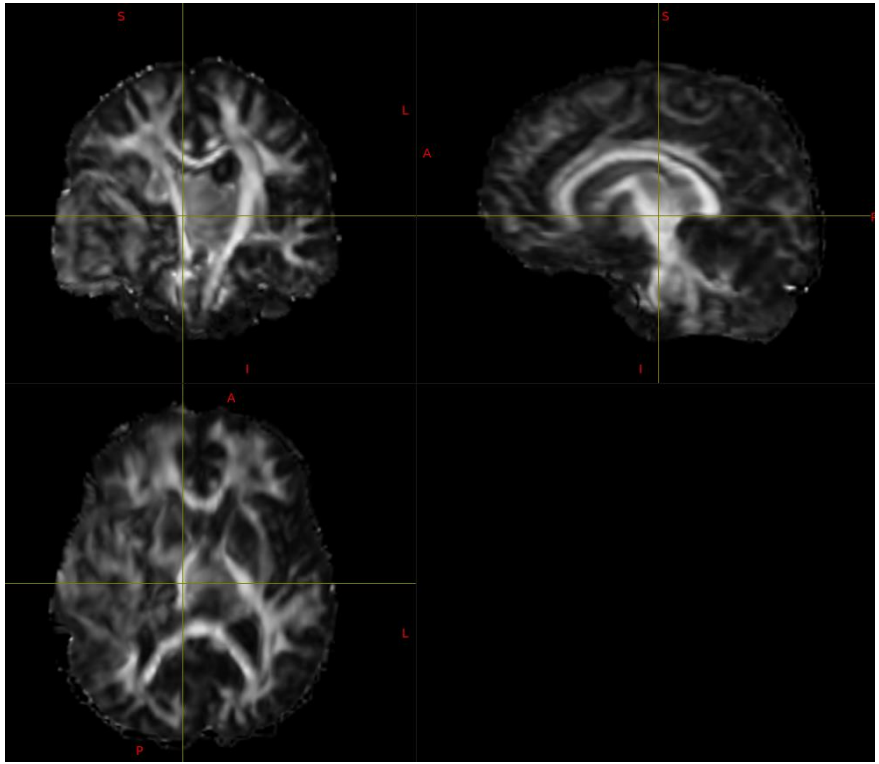
T1 + FA NRR



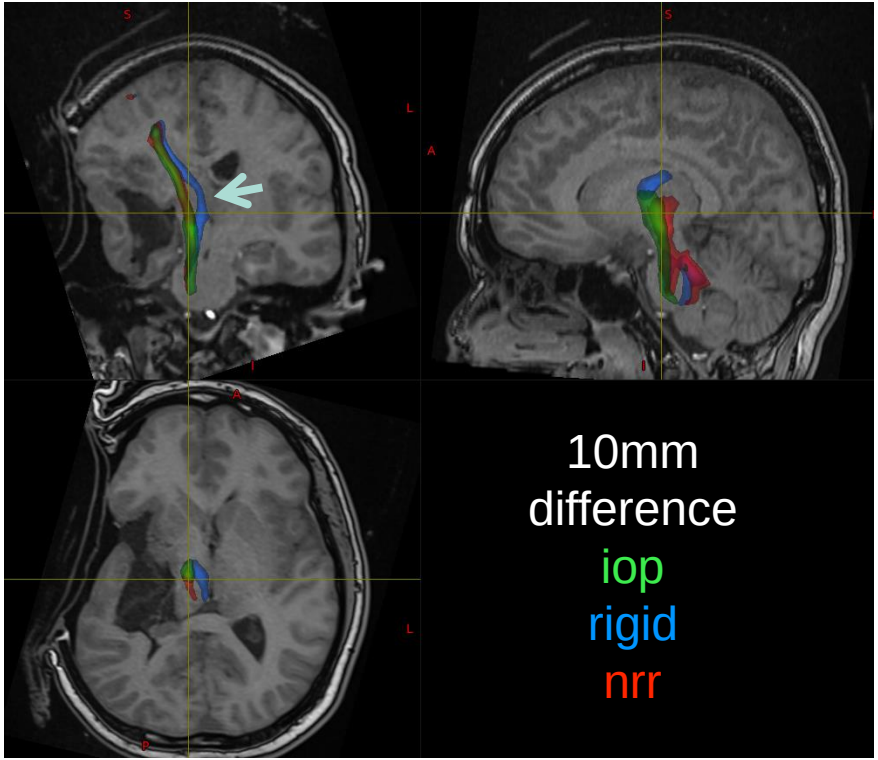


T1 + FA NRR





CST – L Hand M1



Dice score:

rigid vs iop = 0.21

rigid vs nrr = 0.19

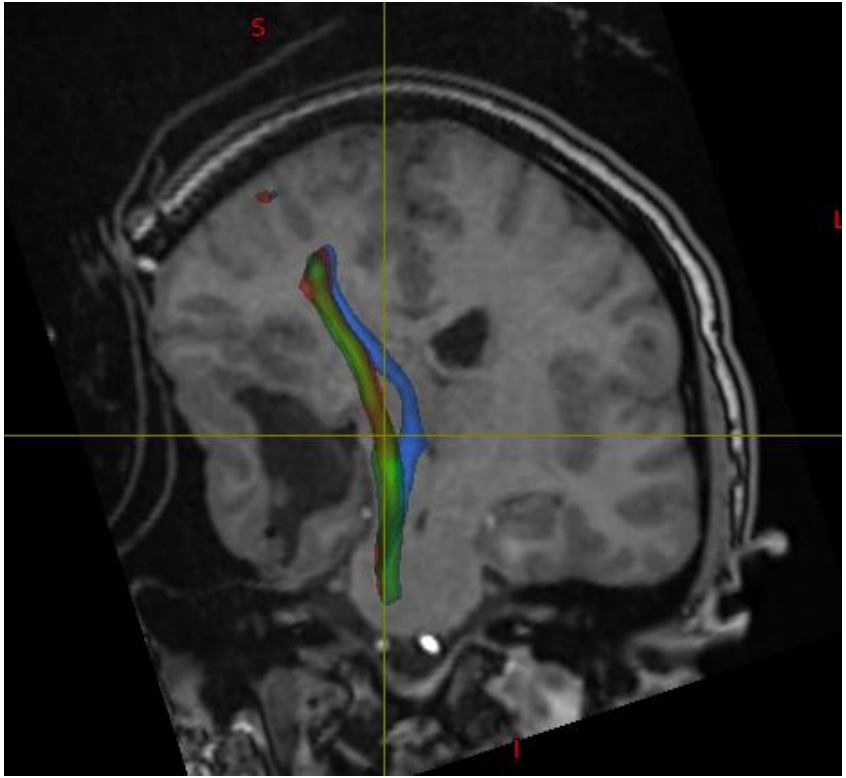
nrr vs iop = 0.47

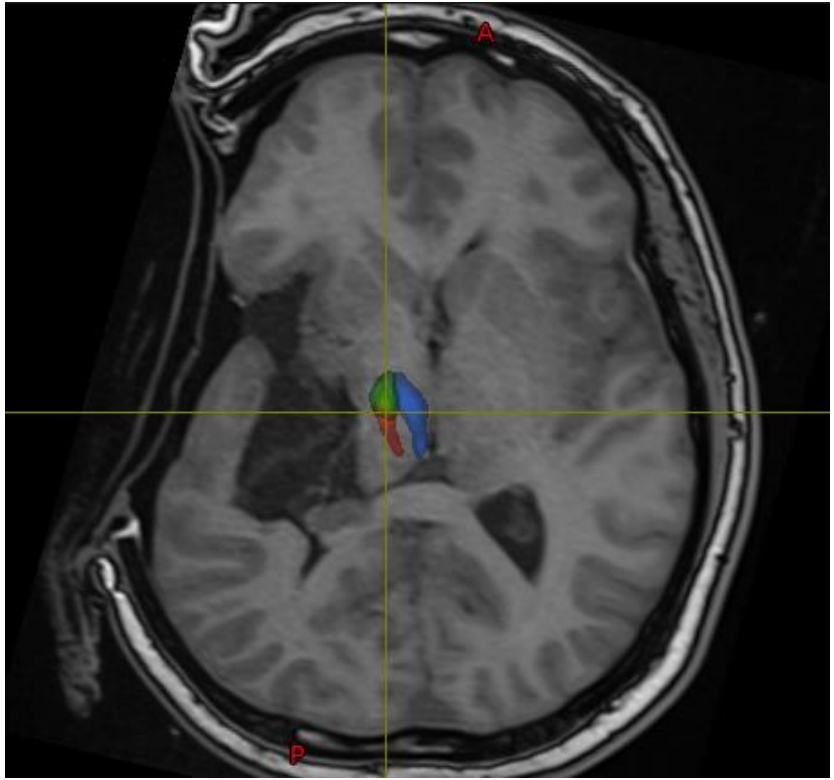
Notice:

- distance from cavity
- differences A-P

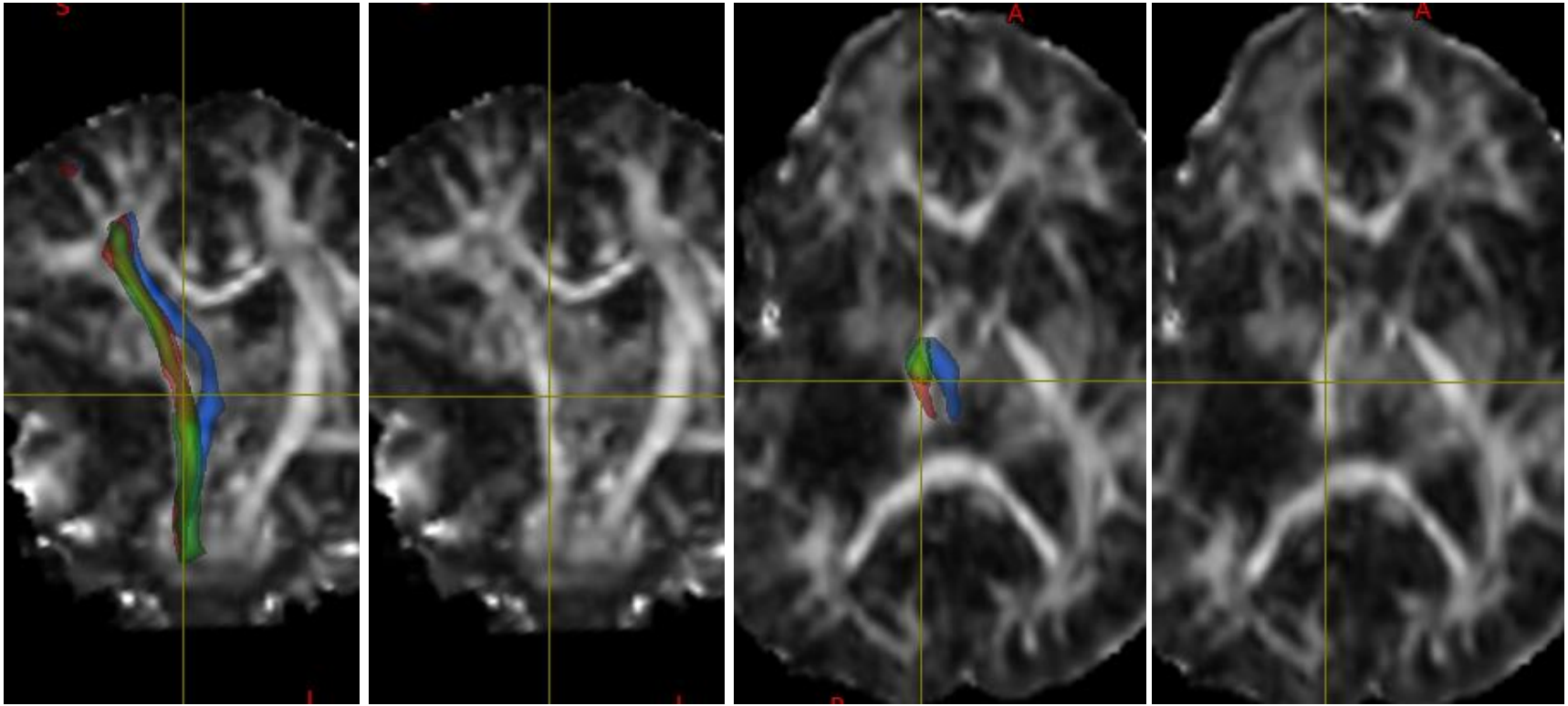
=> usability depends on aim of further surgery

CST – L Hand M1

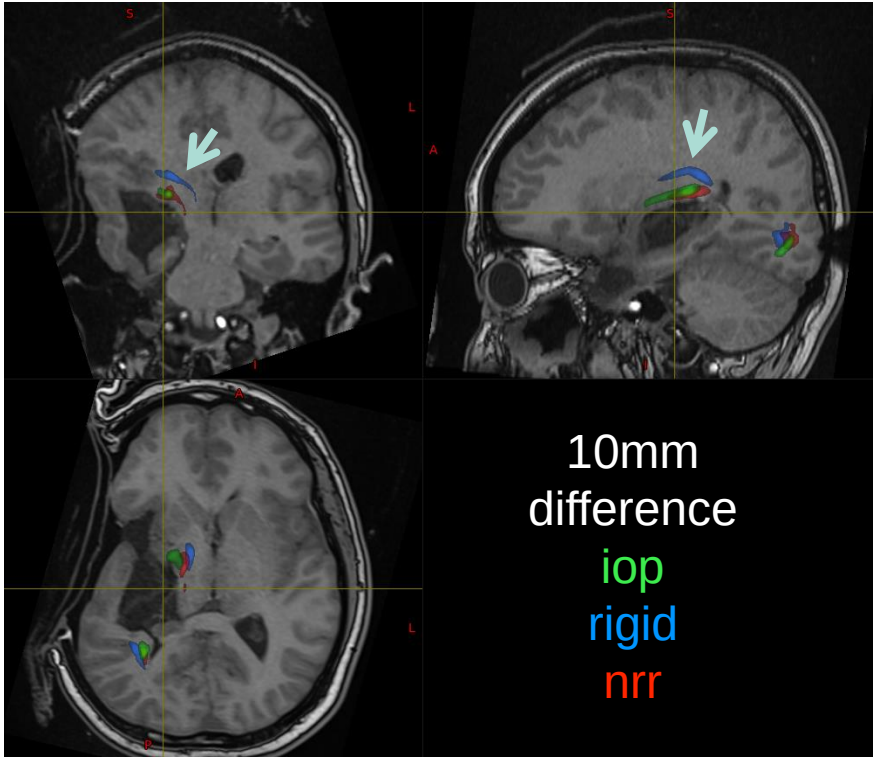




CST – L Hand M1



Optic Radiation



Dice score:

rigid vs iop = 0.07

rigid vs nrr = 0.14

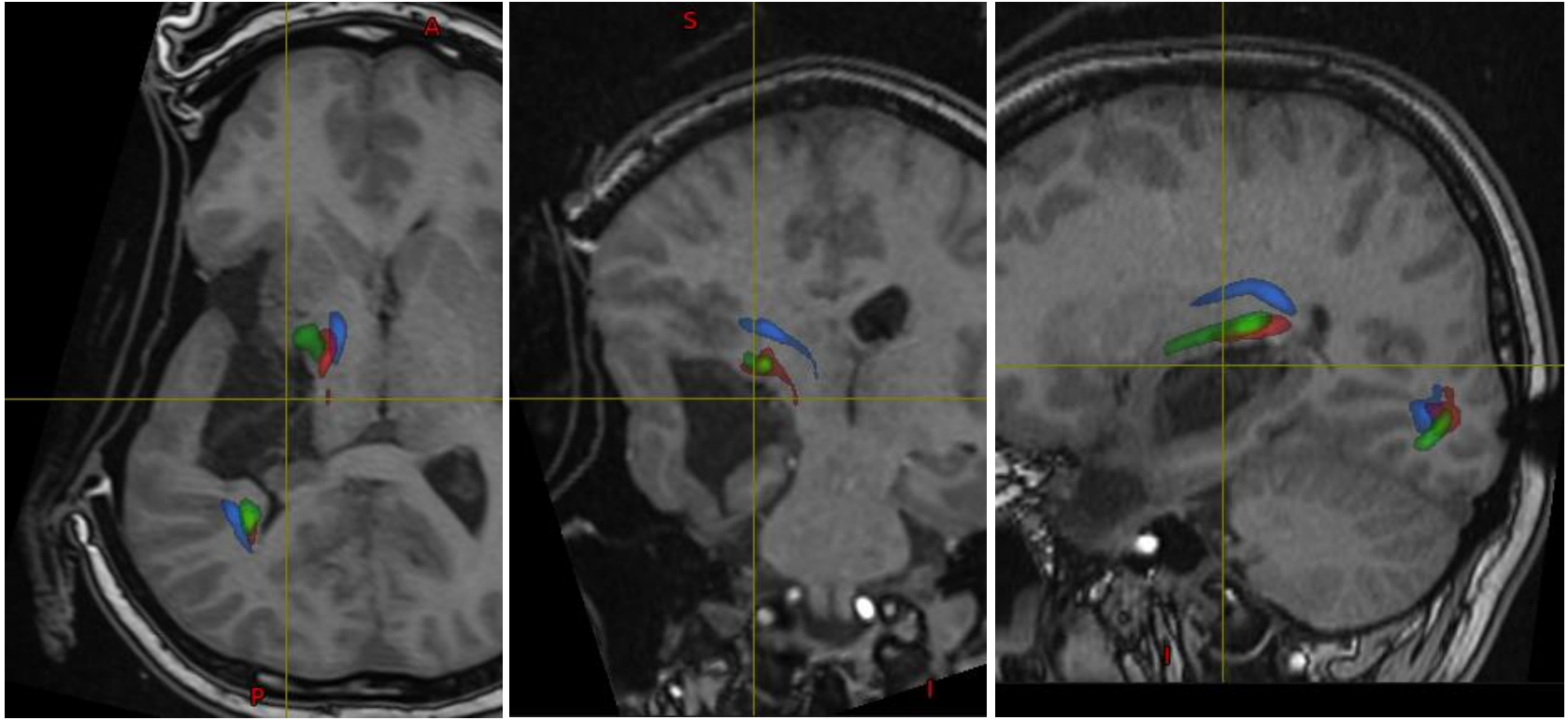
nrr vs iop = 0.31

Notice:

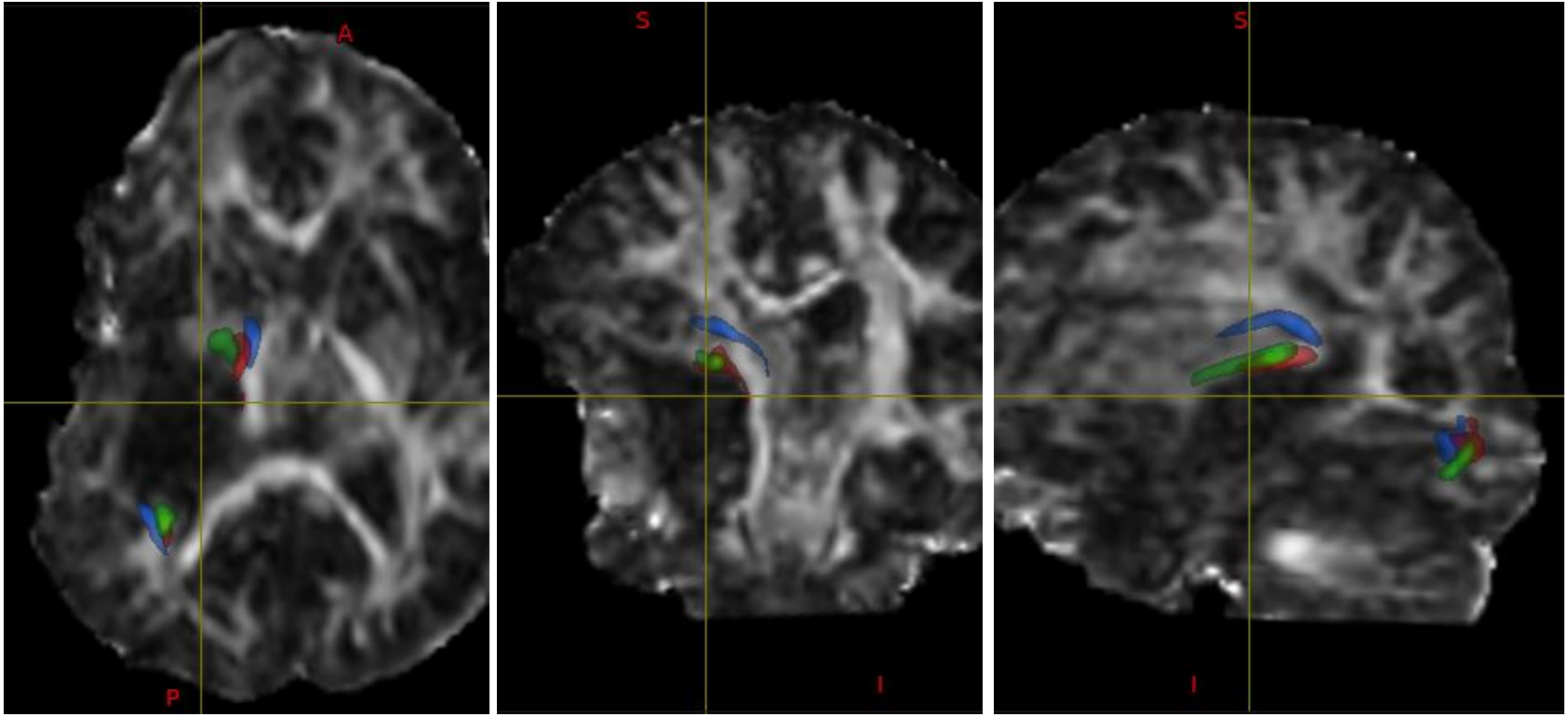
- distance from cavity
- differences A-P, L-R

=> usability depends on aim of further surgery

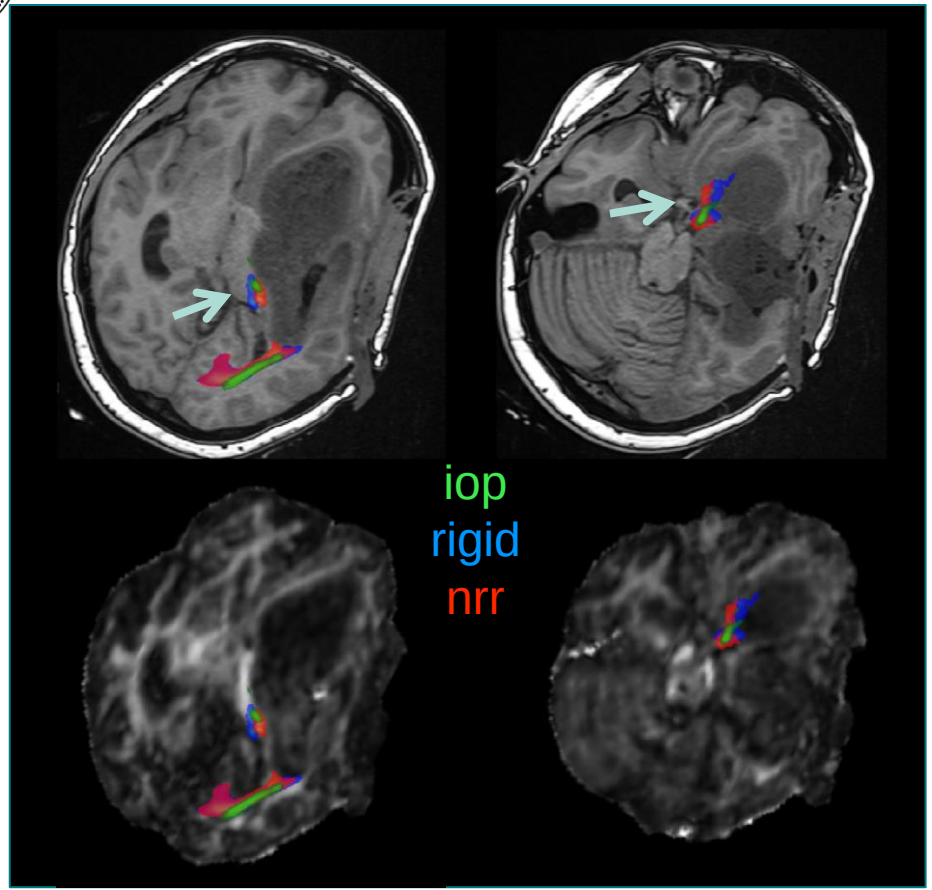
Optic Radiation



Optic Radiation



Subject 2: OR



Dice score:

rigid vs iop = 0.34

rigid vs nrr = 0.38

nrr vs iop = 0.45

Notice:

- shift of tracts in opposite directions

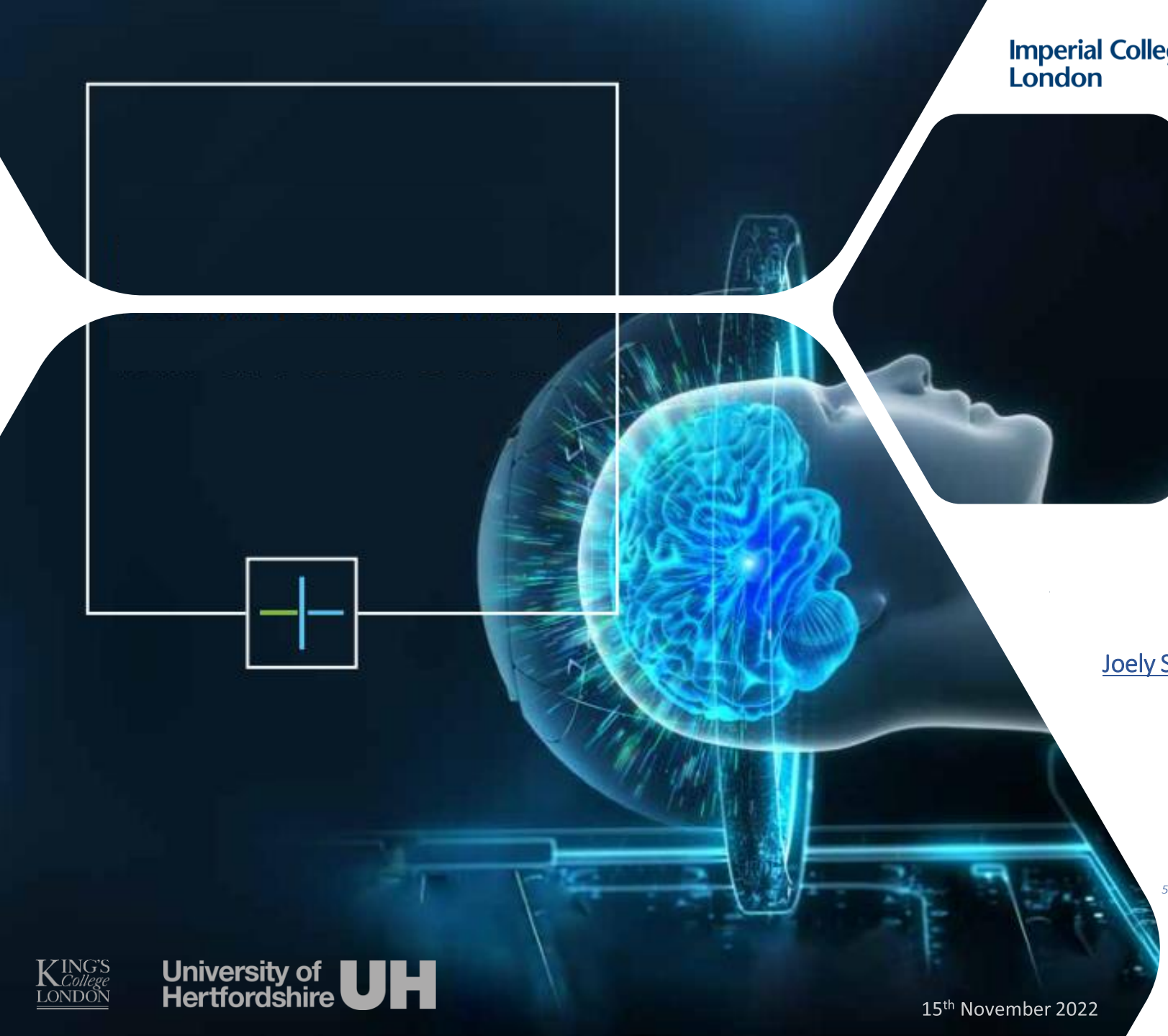
Conclusions

NRR integrating T1 + FA in a unified similarity measure:

- Works much better than rigid and affine registrations
  - It brought tracts in their plausible intra-op anatomical location
- No requirement to model deformation (tumour, brain shift)
- Not clear yet if good enough for clinical use
  - Needs **case–by–case assessment** (surgical aim, neuroradiolgist evaluation…)

Conclusions

- Resulting deformations in both +ve and –ve directions
  - depends on brain shift and tumour resection
- Performed in the time frame available in iMRI
  - ~15–20 min from end of T1+DWI acq to patient back on surgical position, even longer for surgeon to be ready for further surgery
- It can inform the initialisation of algorithms that perform geometric transformation of tracts
- FA could be replaced by WM segmentation (if reliable)



Imperial College London

Imperial College Healthcare NHS Trust

Ultra high-field MRI (7T) of the VIM nucleus to validate 3T diffusion tractography and anatomical targeting for MRgFUS of Essential Tremor

Joely Smith[1,2], Dr Ayesha Jameel[1,3,4], Dr Peter Bain[3,4], Dr Brynmor Jones[1], Prof. Dipankar Nandi[3,5], Rebecca Quest[1,2], Prof. Wladyslaw Gedroyc[1,3]

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King's College London

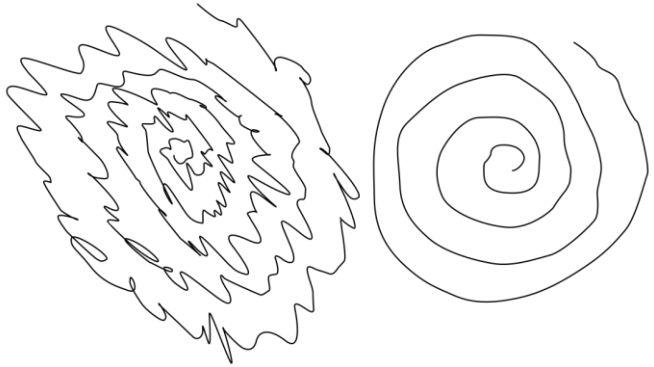
University of Hertfordshire UH

15th November 2022

IPEM: Advanced Neuro MRI

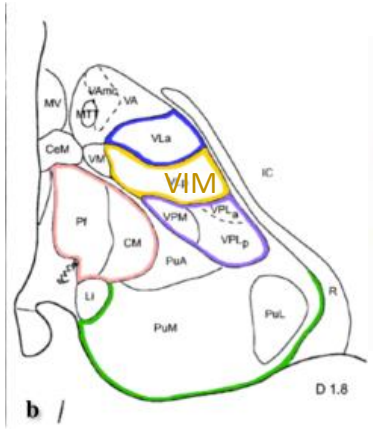
Essential Tremor (ET)

- At our Trust we are performing high-intensity focussed ultrasound (FUS) treatment on patients with ET
- ET is the most common movement disorder worldwide and has a huge impact on patients quality of life
- Kinetic tremor of the upper extremities
- ET is medically refractory in 50% of pts
- Typical treatment for pts is DBS surgery
- But there are on-going health risks associated and it is an invasive surgery



MRgFUS

- MRgFUS – MR guided Focused UltraSound
- FUS is an emerging non-invasive treatment that uses an array of 1024 US elements fixed into a helmet, to propagate US through the skull and into the brain,
  - ➢ where the elements meet at the focal point and accumulate to deposit a large dose of energy
- This ablates a 2-5mm^3 target, **the VIM nucleus** and supresses the tremor
- real-time monitoring with MRI and MR Thermometry provides anatomical thermal mapping using phase shift imaging
- Large multi-disciplinary team
- Low quality MR brain imaging



MRgFUS

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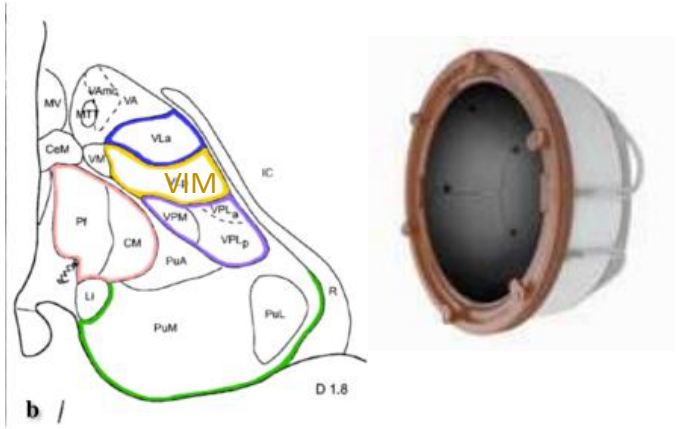
- Large multi-disciplinary team
- <u>Low quality MR brain imaging</u>

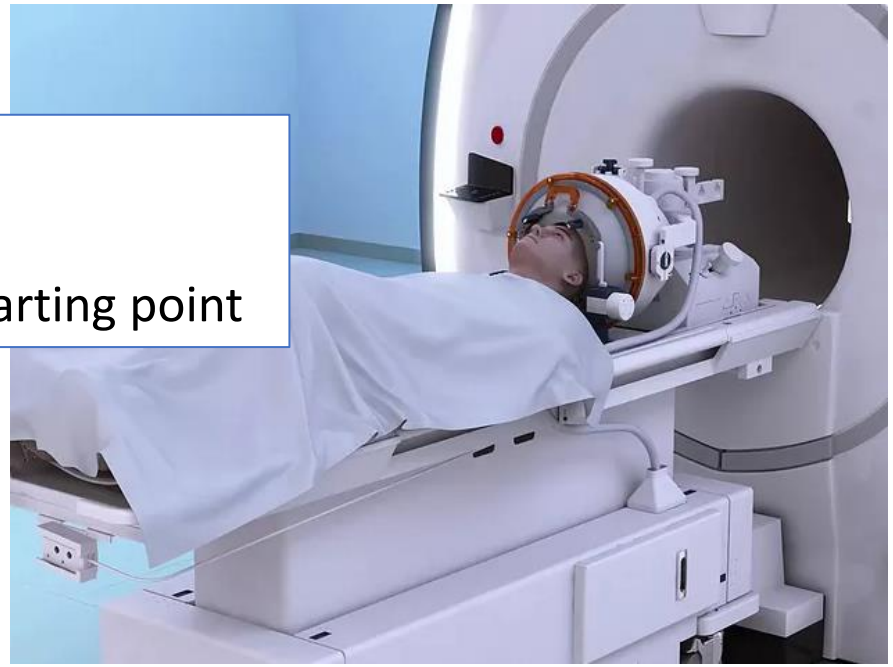


MRgFUS - Treatment

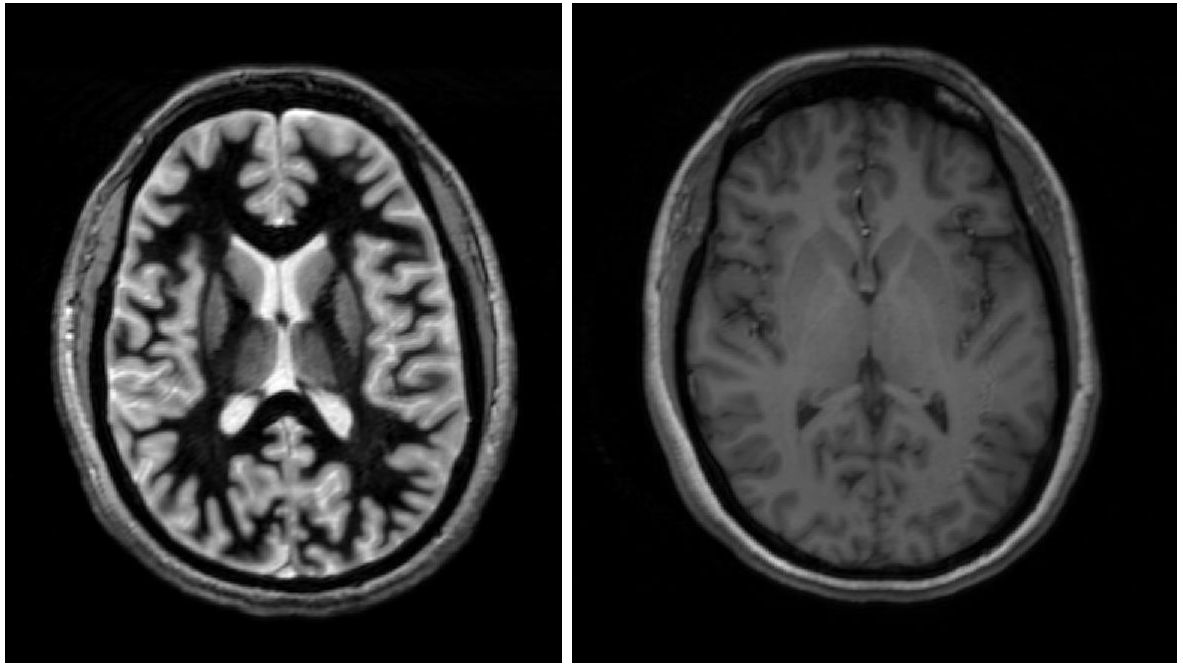
- 2-5mm target in the brain – The VIM nucleus

- Pre-procedure imaging
  - FGATIR and CT fused to low SNR images
  - Anatomical landmarks and geometric measures guide the starting point

- MR-guided & MR Thermometry
  - But the US helmet is big
  - Therefore limited to imaging with the integrated body coil
  - Poor image quality



Pre-procedure MRI



FGATIR MPRAGE

Neuroimage. 2009 Aug;47 Suppl 2:T44-52. doi: 10.1016/j.neuroimage.2009.04.018. Epub 2009 Apr 10.

A high resolution and high contrast MRI for differentiation of subcortical structures for DBS targeting: the Fast Gray Matter Acquisition T1 Inversion Recovery (FGATIR)

Atchar Sudhyadhom [1], Ihtsham U Haq, Kelly D Foote, Michael S Okun, Frank J Bova

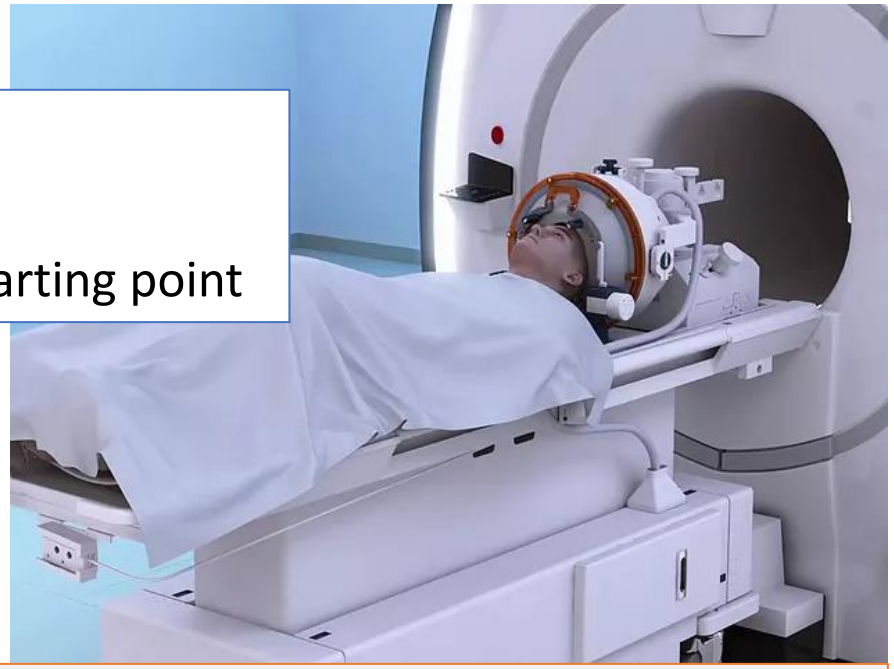
Affiliations + expand

PMID: 19362595 DOI: 10.1016/j.neuroimage.2009.04.018 Sign in

	T1-w 3D MP-RAGE	T2-w 3D FLAIR	T1-w 3D FGATIR
Repetition time (TR)	1600 ms	6000 ms	3000 ms
Echo time (TE)	4.38 ms	353 ms	4.39 ms
Inversion time (TI)	800 ms	2200 ms	409 ms
Inversion pulse angle	90°	180°	180°
Matrix	384 × 288	256 × 240	320 × 256
Field of view (mm)	256 × 192	256 × 240	256 × 192
Slices	160 × 1 mm	160 × 1 mm	160 × 1 mm
Orientation	Axial	Sagittal	Axial
Bandwidth	130 Hz/Px	1302 Hz/Px	130 Hz/Px
Acquisition time	6:45 min	12:08 min	11:14 min

MRgFUS - Treatment

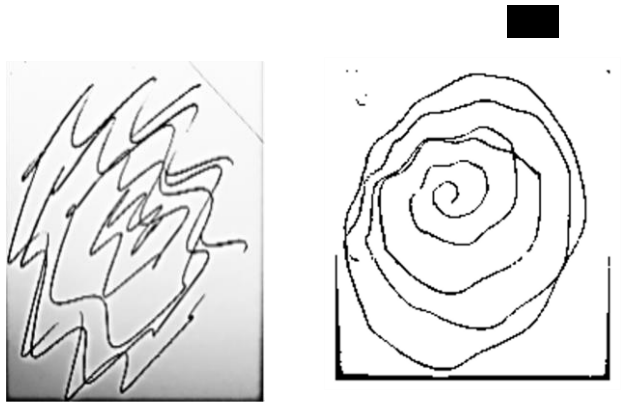
- 2-5mm target in the brain – The VIM nucleus

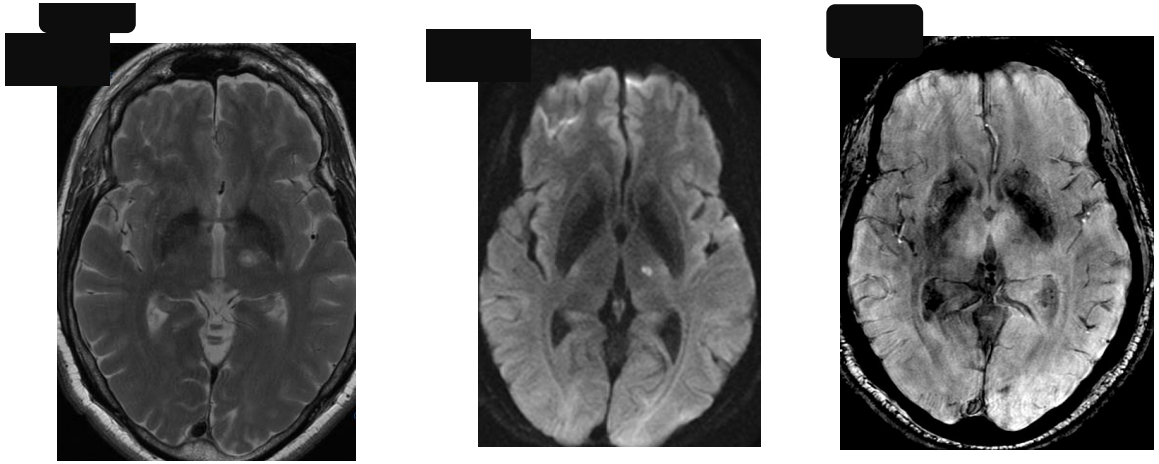


- Pre-procedure MR imaging
  - FGATIR and CT fused to low SNR images
  - Anatomical landmarks and geometric measures guide the starting point
- MR-guided & MR Thermometry
  - But the US helmet is big
  - Therefore limited to imaging with the integrated body coil
  - Poor image quality
- Feedback treatment
  - Test sonications with sub-ablative doses are delivered
  - Consultant Neurologist tests pt with a few exercises e.g. spiral drawing
  - Once located region, tissue receives large dose (MR Thermometry ensures the key temperature is reached, 56^{o}C)

MRgFUS - Treatment

- Small region, the VIM nucleus, is ablated
- Successful permanent damage, tremor suppressed!



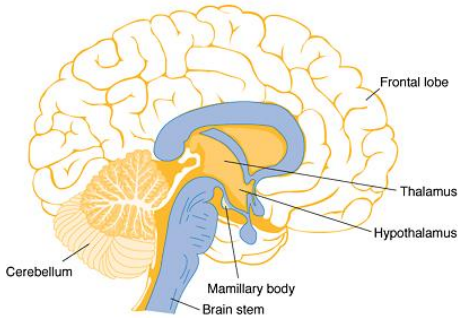


VIM nucleus

- Primary target for MRgFUS treatment of ET
- Historically targeted by DBS, gamma knife and RF ablation

- Function:
  - Thalamic motor nucleus
  - Relays basal ganglia, cerebellum and motor cortex
  - Key role in tremor

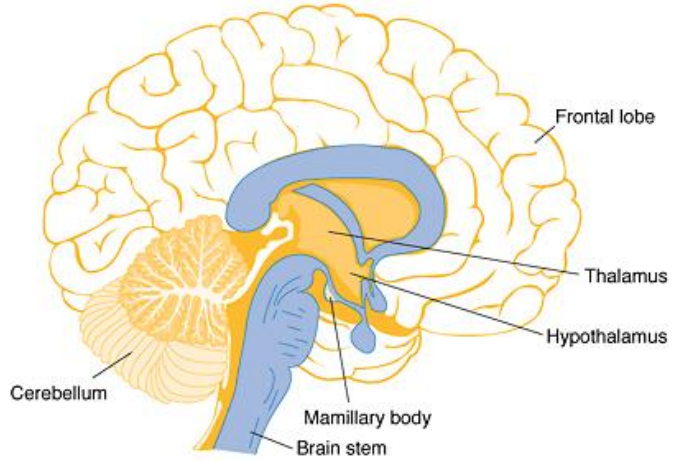
- Position:
  - Anterolateral and inferior within thalamus
  - Measures approximately[1]:
    - 2-4 mm anterio-posterior
    - 4-6 mm medio-lateral
    - 7-10 mm superior-inferior



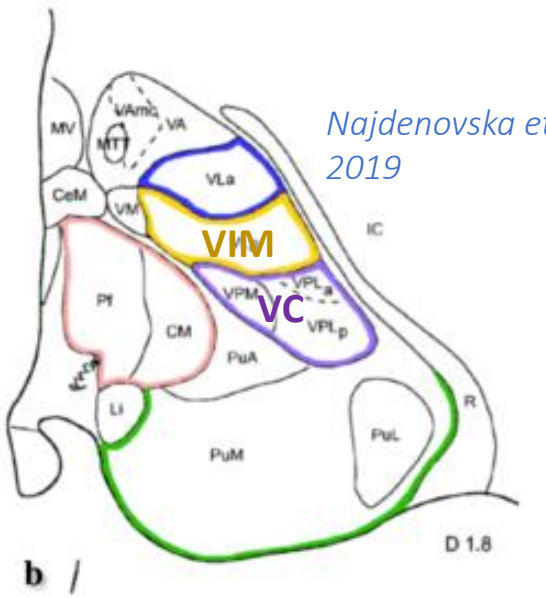
VIM nucleus on Schaltenbrand Wahren Atlas

VIM nucleus

- important adjacent structures risk adverse effects[2]
  - ➢Ventral Caudalis (VC) - sensory
  - ➢Internal Capsule (IC) - motor



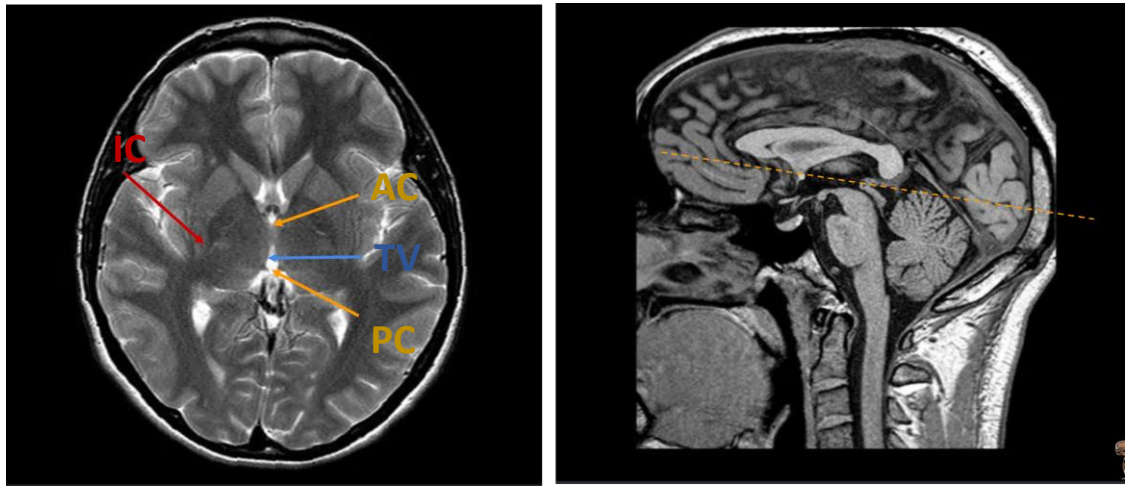
- cannot be directly visualised on current clinical scanners (1.5T and 3T)
- most accurate approach VIM targeting under debate…



Najdenovska et al. 2019

Current standard approach to VIM targeting

- The most commonly used targeting method is landmark-based
- Using stereotactic landmarks to infer VIM position:
  - anterior commissure - posterior commissure line (AC-PC)
  - third ventricle (TV)
  - internal capsule (IC)



- These pre-set geometric measurements are used for every patient

- At our institution (in 2022):
  - AP: 30% of AC-PC distance anterior to PC
  - ML: 2mm medial to IC
  - SI: 2mm above the AC-PC line

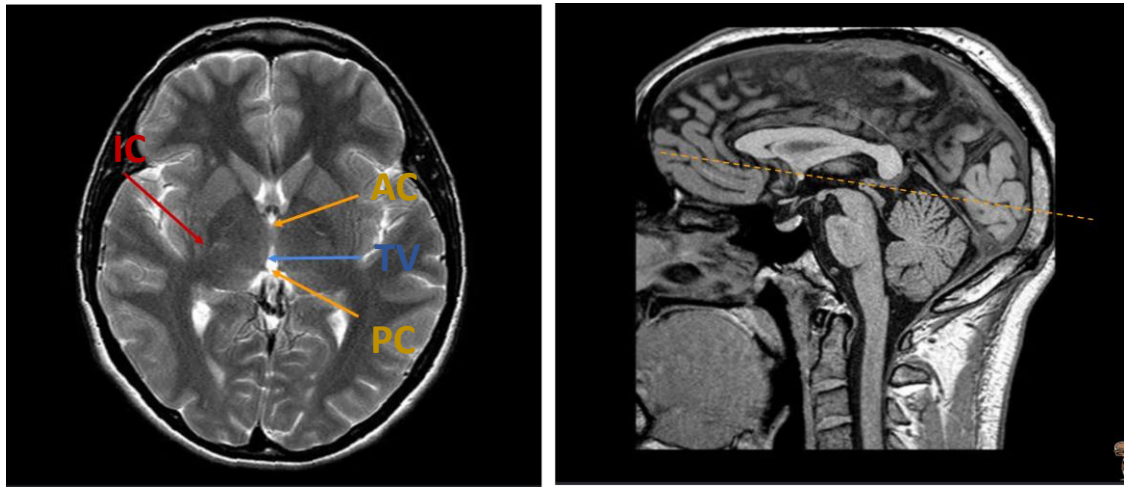
Current standard approach to VIM targeting

Imperial College Healthcare NHS Trust

Imperial College London

PROs OF ANATOMY BASED TARGETING

- To date good tremor suppression
- Acceptable safety profile
- Quick, reproducible and doesn't require additional technology/expertise



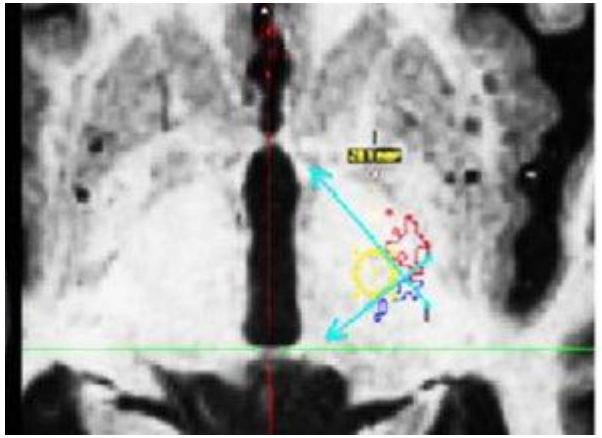
CHALLENGES OF ANATOMY BASED TARGETING

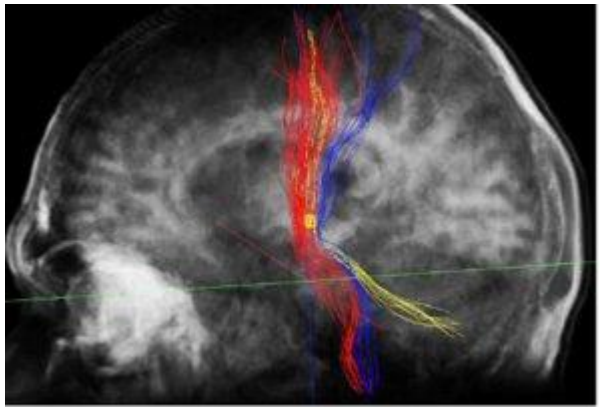
- Not patient specific - does not consider natural variation in neuroanatomy[3]
- No further safety information acquired

Tractography-based targeting

- An emerging method for VIM targeting is tractography based targeting
- noninvasive imaging based on motion of water or “diffusion” demonstrates the brain’s white matter pathways

- Technique well described by Sammartino et al[3]
- VIM position is inferred by locating three key tracts
  - Pyramidal Tract (PT)
  - Medial Lemniscus (ML)
  - Dentorubrothalamic tract (DRT)





Sammartino et al. 2016[3]

Research question

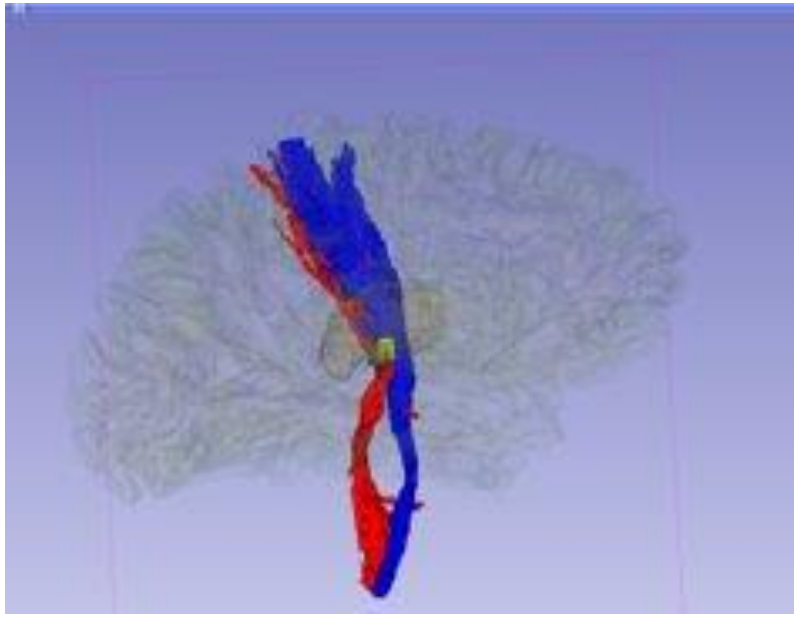
What is the best method to target the VIM?

How can we confirm the accuracy (or inaccuracy) of our current targeting approach?

Could DTI improve our targeting approach?

To improve:

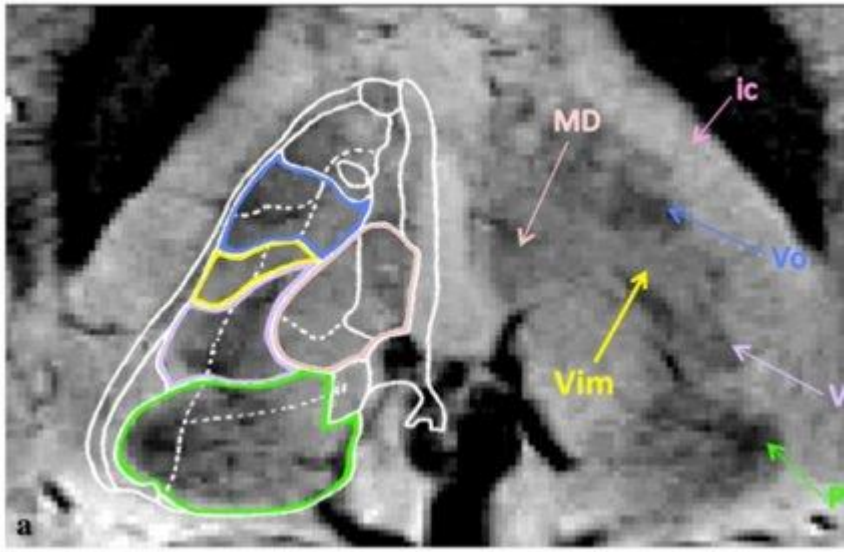
- **Outcomes**
- **Treatment duration**
- **Number of sonications**
- **Risk of adverse effects**



VIM on 7T

- VIM can be discerned on 7T susceptibility weighted imaging (SWI)
- Demonstrated by Najdenovska et al. 2019[2]
- VIM has relatively low signal and is distinct from adjacent nuclei, allows direct visualisation

- London Collaborative Ultra-High field System (LOCUS)
- Siemens MAGNETOM Terra – 7T MRI scanner
- Collaboration between several London institutions
  - *Kings College London*
  - *Guys and St Thomas's Trust*
  - *University College London, Imperial College*
  - *The Institute of Cancer Research*



Najdenovska et al. 2019

Aims

The aims of this study were to compare the inferred position of the VIM by our institutions 3T anatomical and 3T tractography methods of targeting against the directly visualised location of VIM on 7T SWI.

In order to review the accuracy of our current targeting methods

Methods

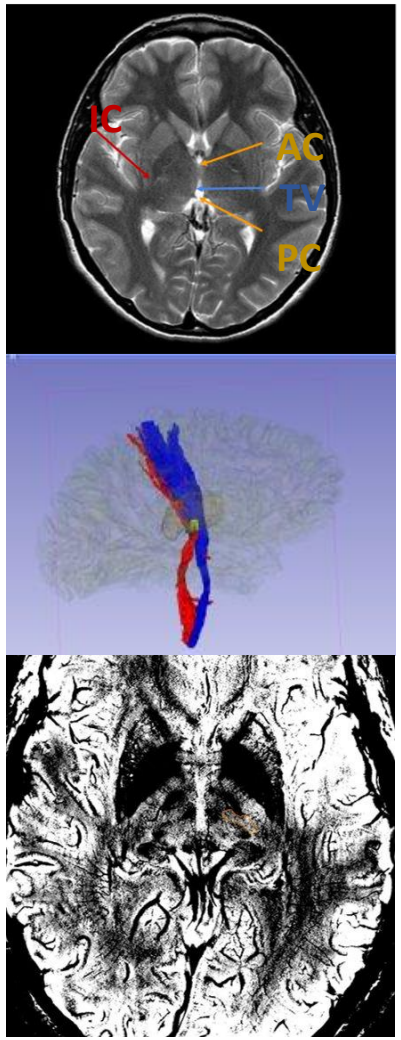
Imperial College Healthcare NHS Trust

Imperial College London

- 3 healthy volunteers were scanned on 3T and 7T MRI
  - ➢(2F, 1M, mean age: 30.7 ± 2.5 years)

For each healthy volunteer, the VIM was delineated:

- On 3T MR imaging
  - ➢using our institution's current landmark method: **VIM-A**
  - ➢using the tractography methodology: **VIM-T**
- On 7T MR imaging
  - ➢by direct visualisation on contrast optimised SWI: **VIM-S**



VIM-A

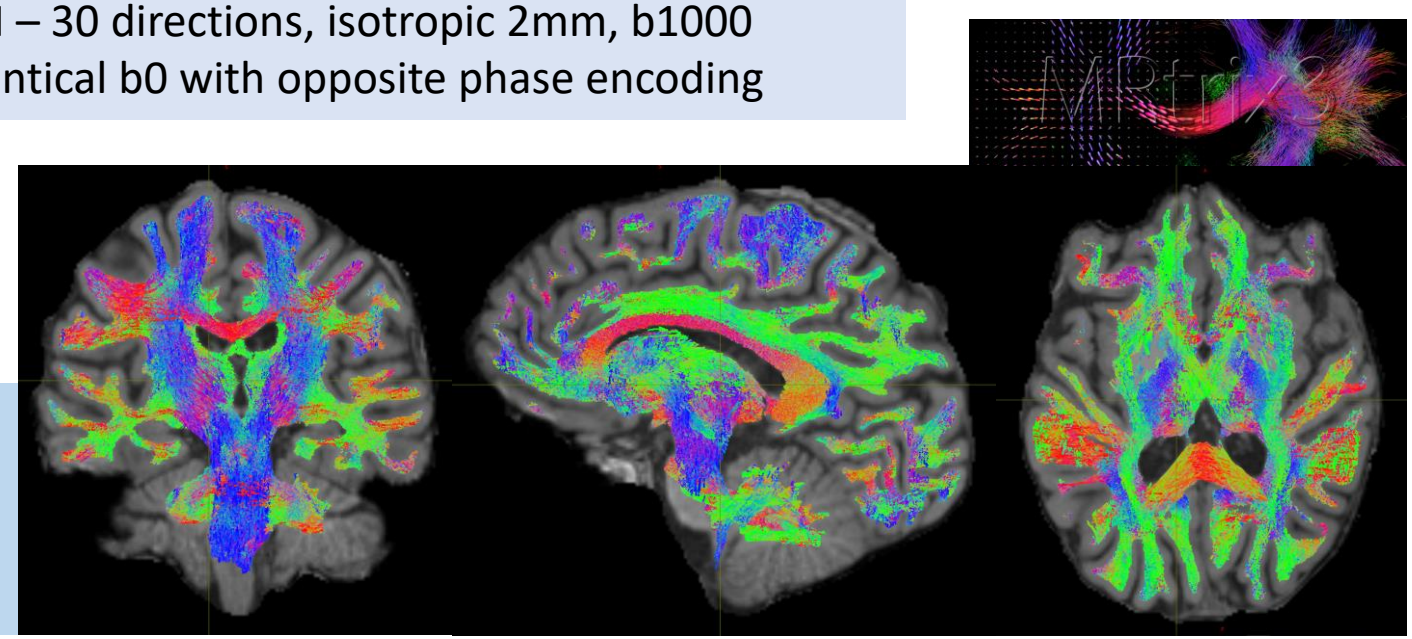
VIM-T

VIM-S

Methods – 3T imaging

3T clinical (Siemens Verio) protocol:

- 3D MPRAGE
- 3D T2 FLAIR
- 3D FGATIR
- DTI – 30 directions, isotropic 2mm, b1000
- Identical b0 with opposite phase encoding



DTI processing:

- MRTrix3 (v3.0.1)
- spherical deconvolution
- probabilistic streamlines

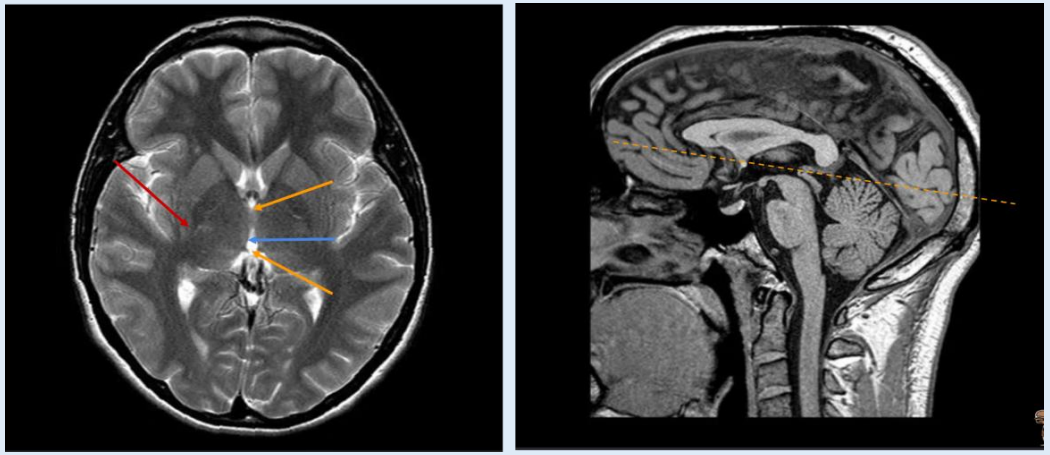
Methods – 3T imaging

Imperial College Healthcare NHS Trust

Imperial College London

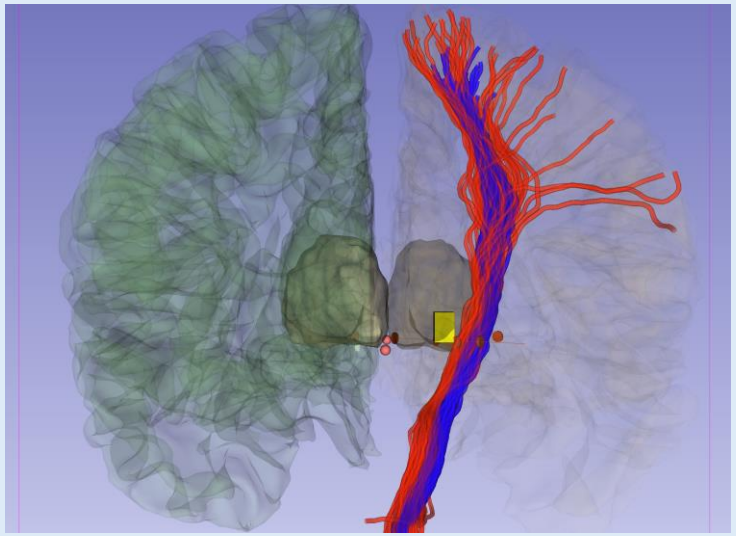
Anatomical landmark method (VIM-A)

- AP: 30% of AC-PC distance anterior to PC
- ML: 2mm medial to IC
- SI: 2mm above the AC-PC line



Tractography method (VIM-T)

- 3 mm from medial and anterior borders of PT and ML (at level of ACPC)
- 4 mm^2 ROI place on axial ICP slice, extended 6 mm superiorly to create VIM-T
- The centre of mass is calculated 3 mm above ACPC



Methods – 7T imaging

Imperial College Healthcare NHS Trust

Imperial College London

7T research (Siemens Terra) protocol:

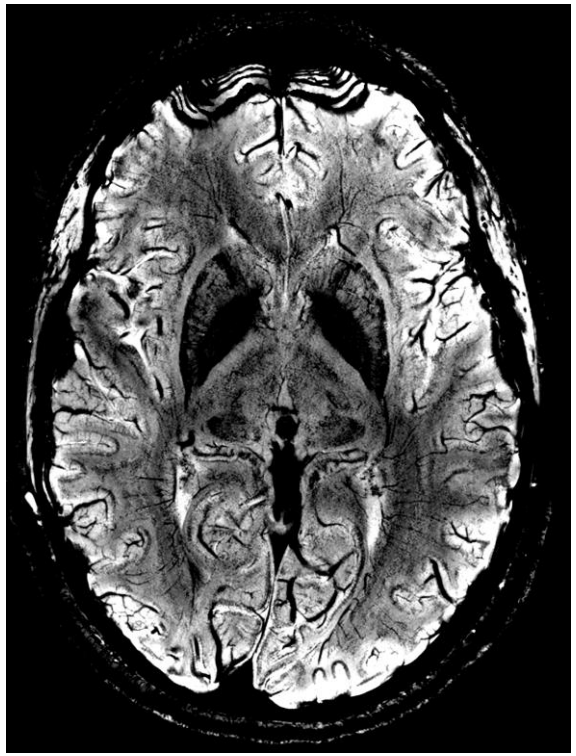
- 3D MP2RAGE
- Dark fluid SPGR
- fl3D VIBE
- T2*
- SWI
- DTI – 64 directions, b1000

7T contrast optimised SWI methodology (VIM-S):

- imaging reviewed and VIM manually delineated on the SWI using Philips Vue PACS workstation
- delineated performed by a Neuroradiologist (AJ)
- verified by a second Neuroradiologist (BJ)
- VIM-S was segmented on 3D Slicer
- centre of mass was calculated

MATLAB®

SWI processing and statistics (R2018b, mathworks)



Methods – VIM comparison

- All imaging was co-registered using FSL's FLIRT linear registration function

- The VIM-A coordinate and VIM-T volume where overlaid onto 7T MRI for visual assessment
- dice similarity analysis was performed between the volumes VIM-T and VIM-S (reference volume)
- The centre of mass coordinates for the two volumes and the VIM-A coordinate were compared

- And the distances in the three planes and the absolute distance were produced

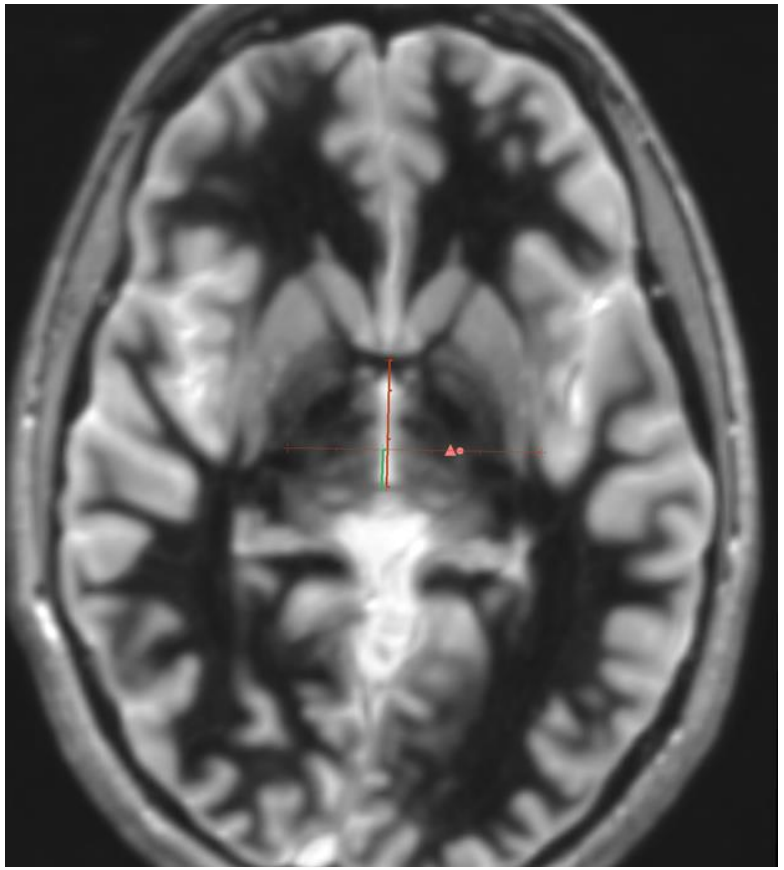
Results

For all 3 healthy volunteers:

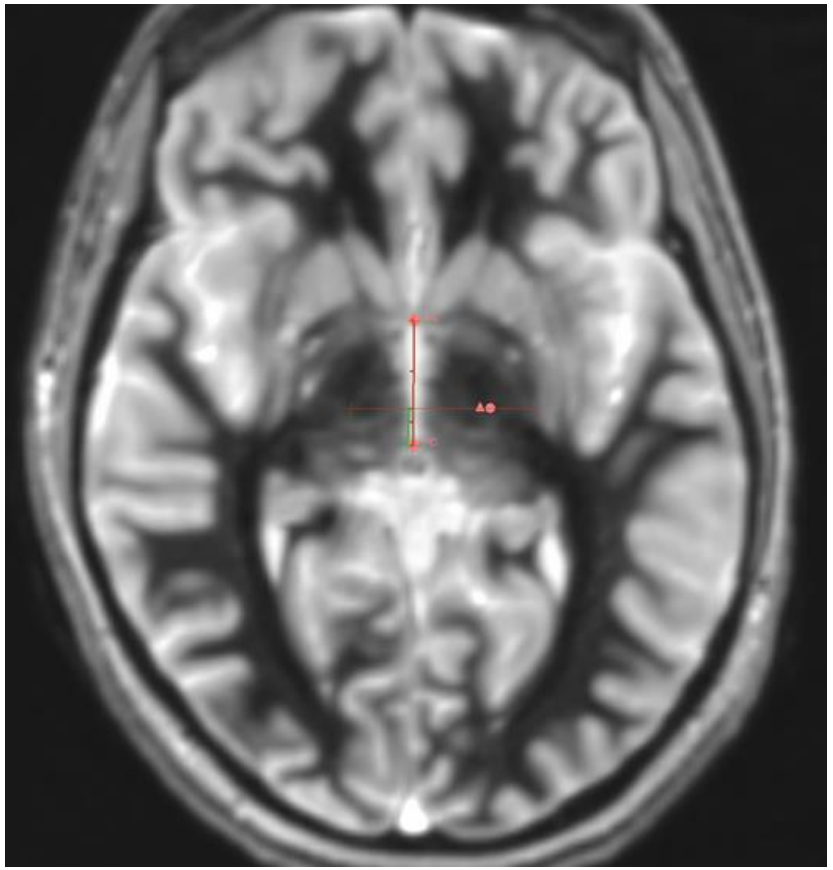
- Imaging was successfully acquired on 3T and 7T MRI including DTI
- VIM was located by anatomical and tractography methods on 3T imaging (VIM-A and VIM-T)
- VIM was located by direct visualisation on 7T SWI sequence (VIM-S)

Results: VIM-A

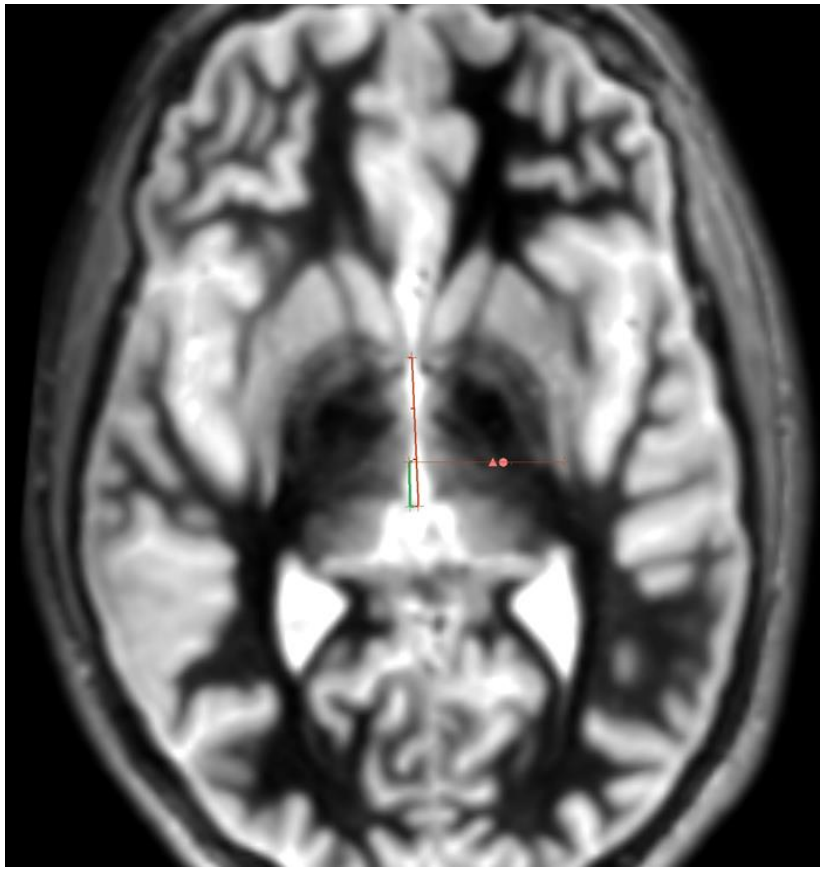
3T Axial FGATIR



HV- 1



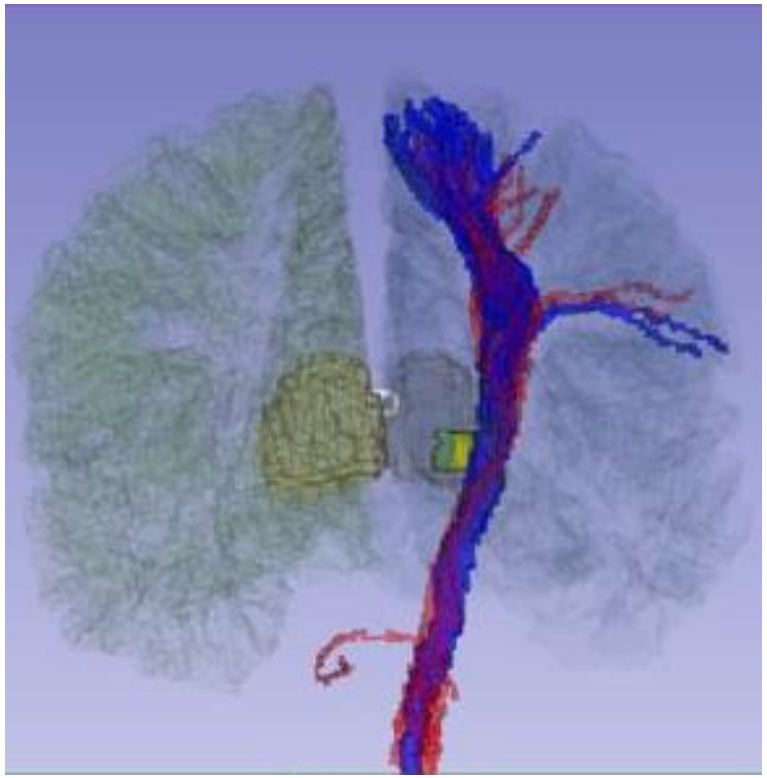
HV- 2



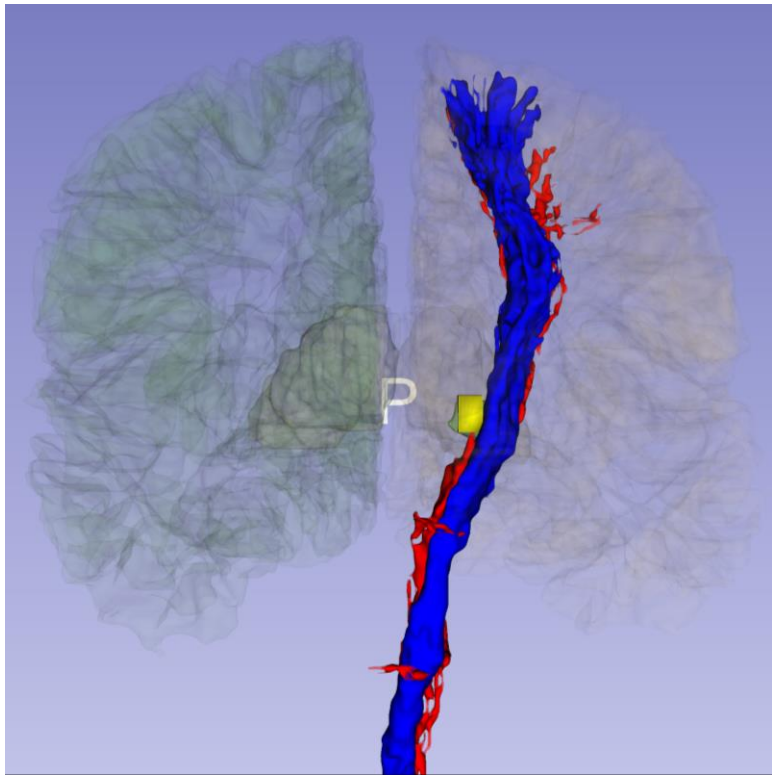
HV- 3

Results: DTI

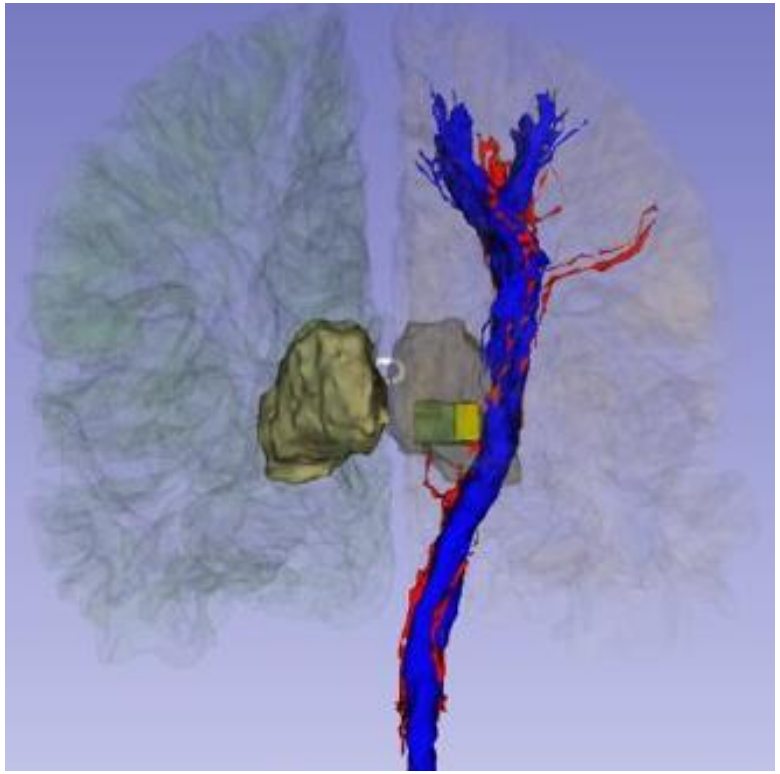
Pyramidal Tract (blue)
Medial Lemniscus (red),
VIM-T (yellow)



HV- 1



HV- 2



HV- 3

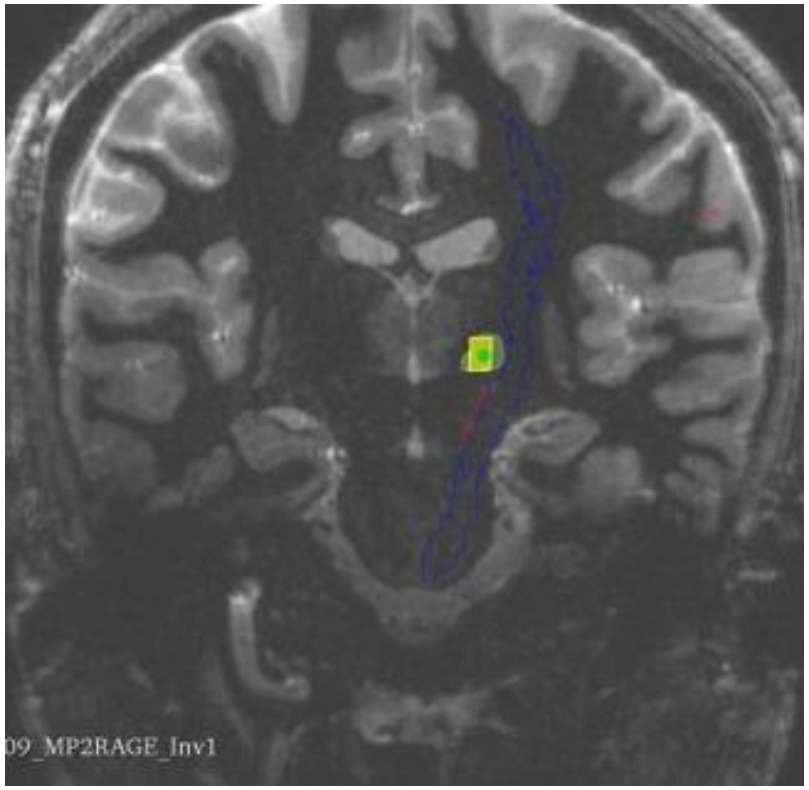
Imperial College Healthcare NHS
NHS Trust

Imperial College London

Results: VIM-T

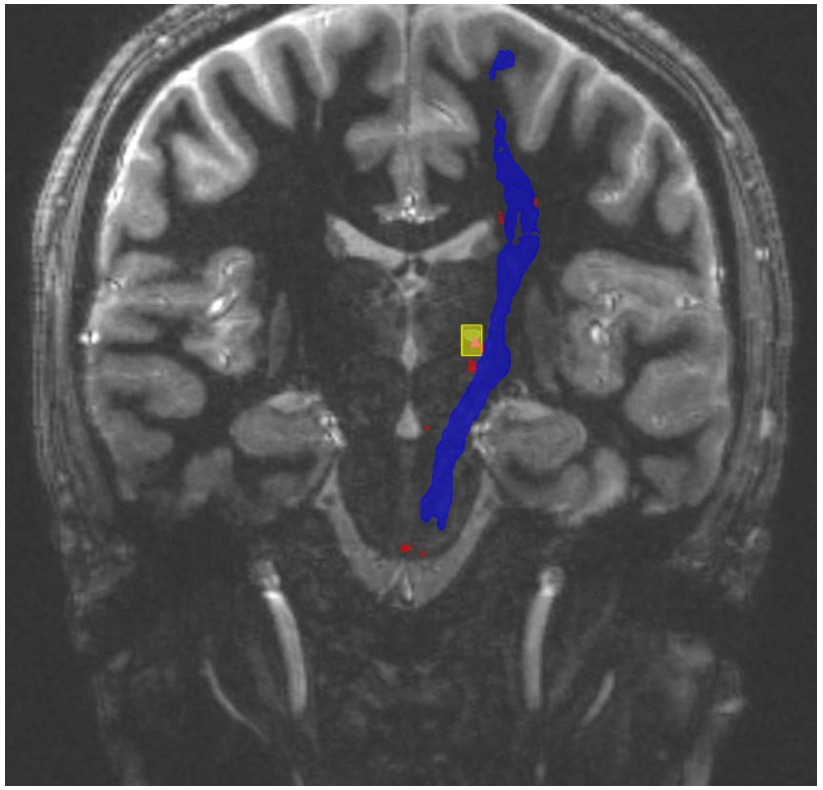
Pyramidal Tract (blue)
Medial Lemniscus (red),
VIM-T (yellow)

HV-1



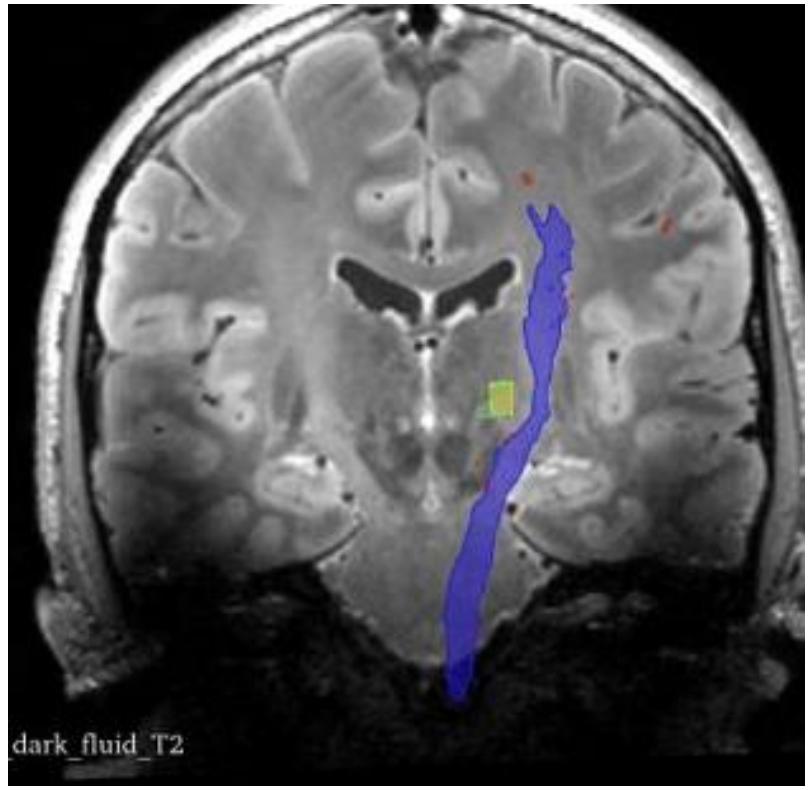
3T Coronal MP2RAGE

HV-2



3T Coronal MP2RAGE

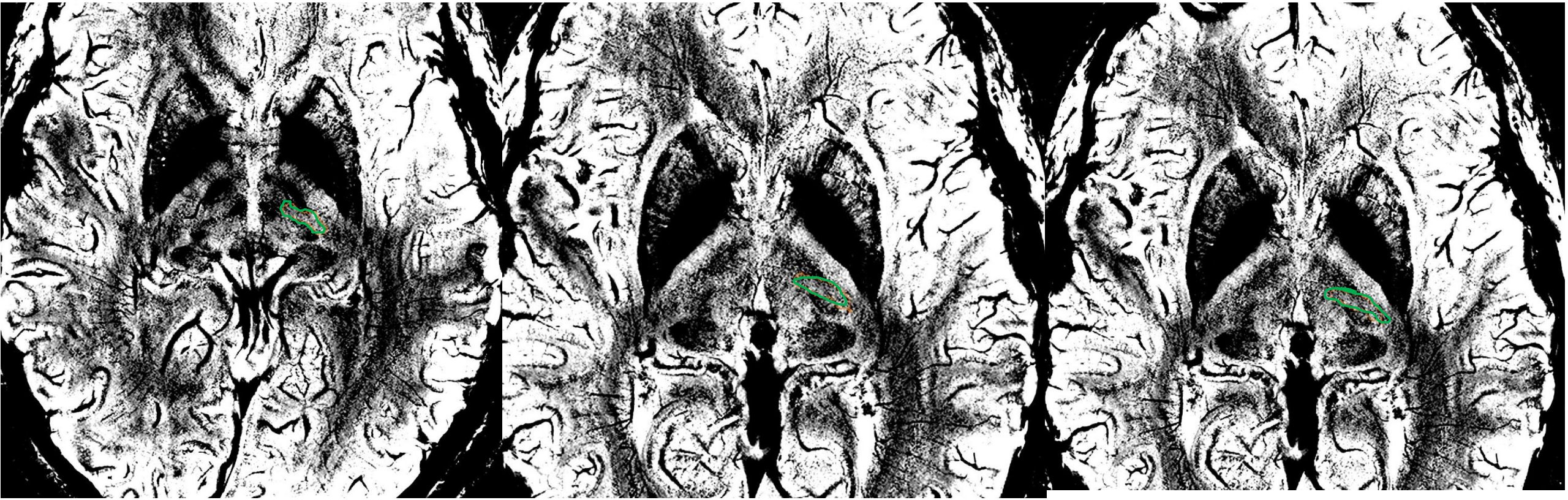
HV-3



3T Coronal FLAIR

Results: VIM-S

7T Axial SWI-CO



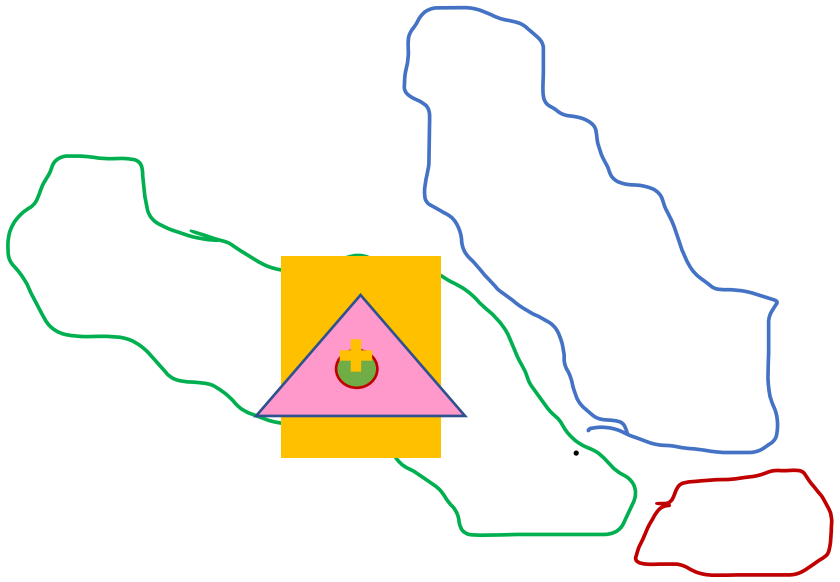
HV- 1

HV- 2

HV- 3

Results: VIM comparison

For each HV, imaging was co-registered and VIM-A & VIM-T were overlayed onto VIM-S



VIM-A

VIM-T

VIM-T centre of mass

VIM-S

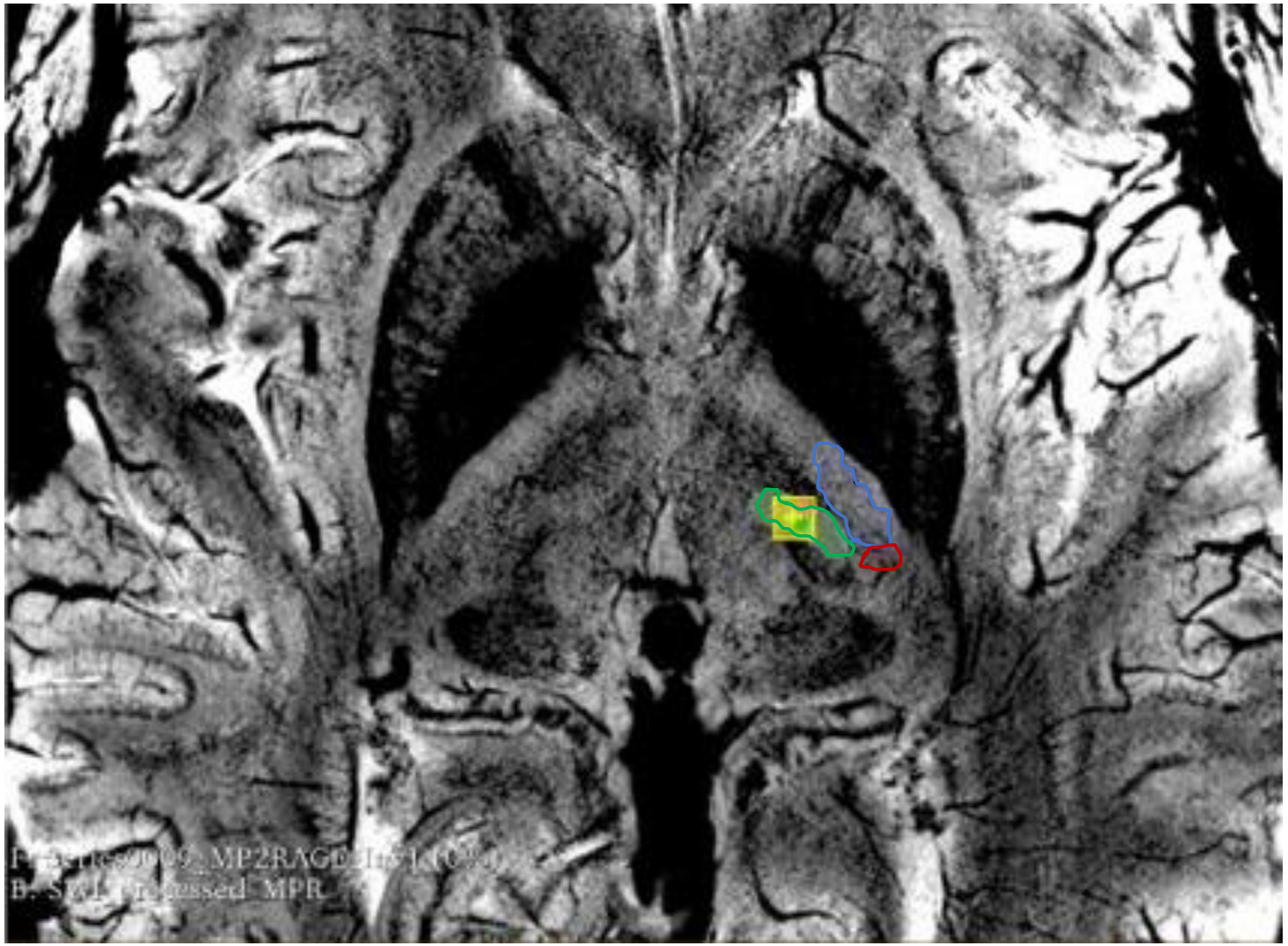
VIM-S centre of mass

Pyramidal Tract

Medial Lemniscus

VIM-A , VIM-T and VIM-S all overlap

HV 1: VIM comparison



VIM-A

VIM-T

VIM-T centre of mass

VIM-S

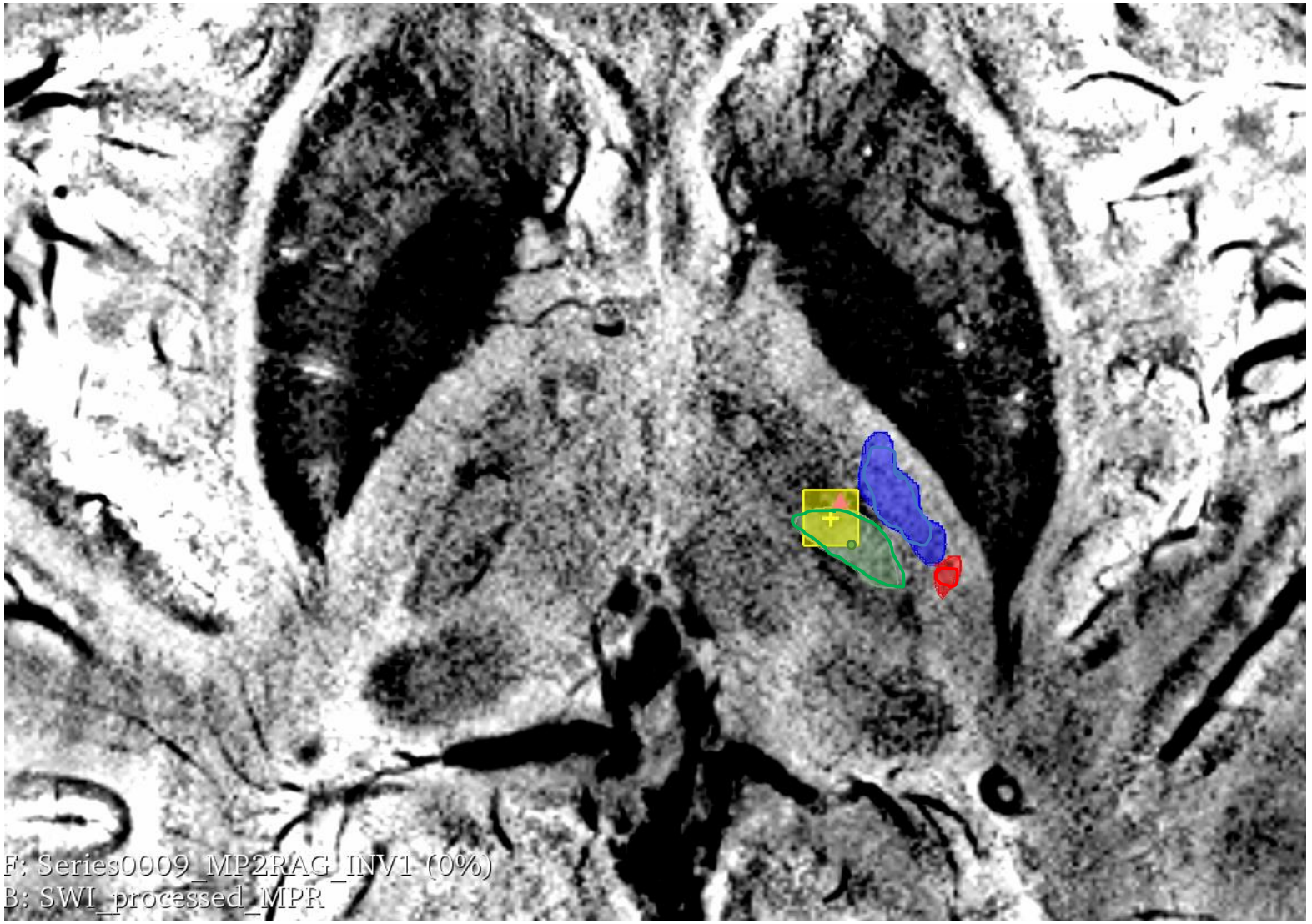
VIM-S centre of mass

Pyramidal Tract

Medial Lemniscus

VIM-A , VIM-T and VIM-S all overlap

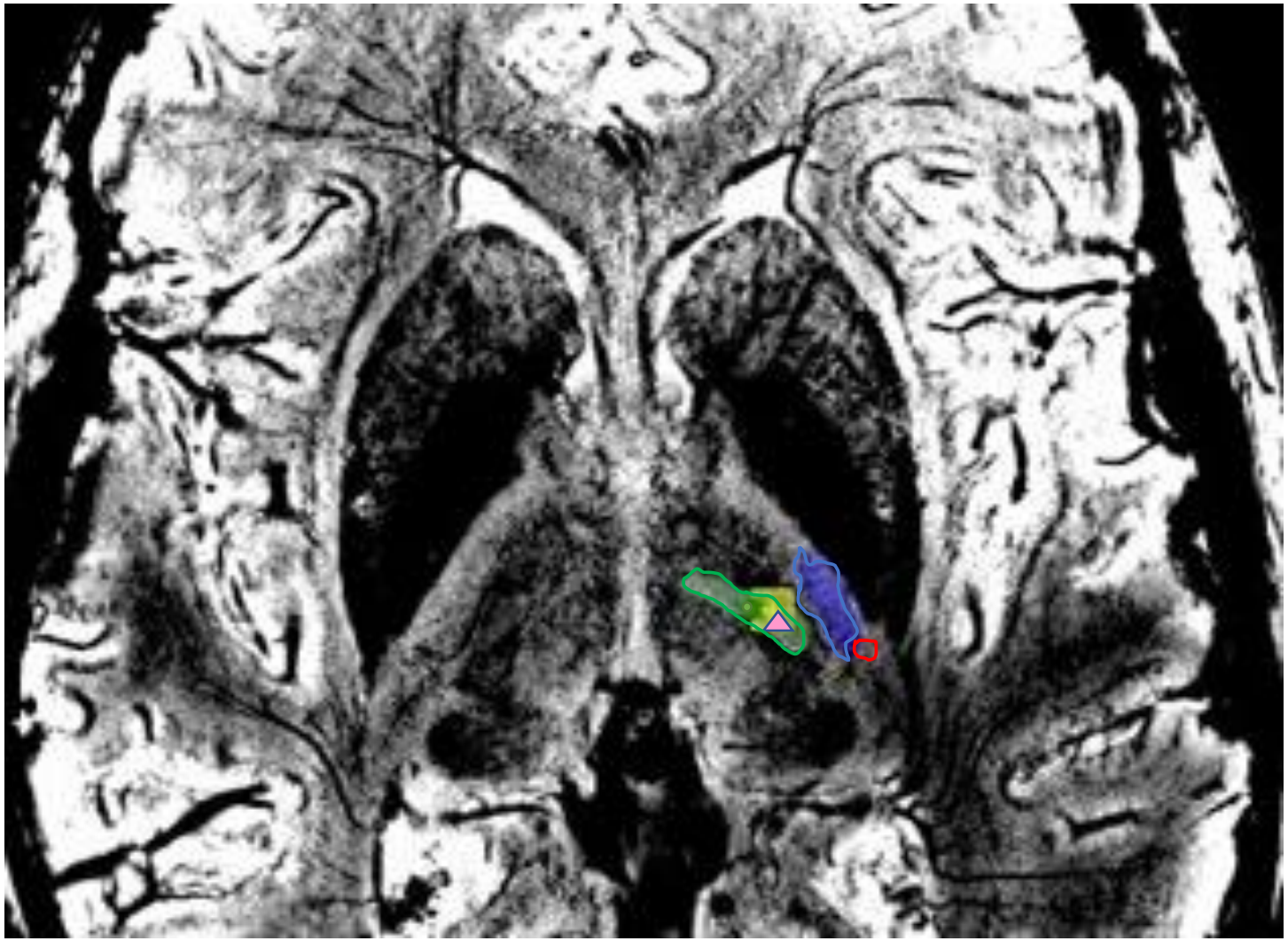
HV 2: VIM comparison



- VIM-A
- VIM-T
- VIM-T centre of mass
- VIM-S
- VIM-S centre of mass
- Pyramidal Tract
- Medial Lemniscus

VIM-T overlaps VIM-A & VIM-S
VIM-A anterior VIM-S

HV 3: VIM comparison



VIM-A

VIM-T

VIM-T centre of mass

VIM-S

VIM-S centre of mass

Pyramidal Tract

Medial Lemniscus

VIM-A , VIM-T and VIM-S all overlap

Results: VIM comparison analysis

Dice coefficient:

- Measure of overlap of volumes
  - 0 = no overlap
  - 1 = perfect overlap
- Compared VIM-S volume to VIM-T volume
- Average dice coefficient of 0.47

Dice testing results: SWI-VIM compared to DTI-VIM

HV	dice coeff	TP (%)	TN (%)	FP (%)	FN (%)	SWI vol (cc)	DTI vol (cc)
1	0.52	11.36	67.29	3.36	17.98	0.19	0.10
2	0.46	10.16	65.75	9.05	15.05	0.13	0.10
3	0.44	7.42	73.43	1.92	17.24	0.26	0.10
average	**0.47**	**9.65**	**68.82**	**4.78**	**16.76**	**0.19**	**0.10**

* where TP, TN, FP, FN are true positives, true negatives, false positives and false negatives, respectively.

Distance to VIM-S centre of mass (mm)

- The target coordinate for VIM-A and VIM-T compared to VIM-S
- The average distance for VIM-A and VIM-T was less than 1mm showing good agreement between techniques.
- This distance is within the expected MRgFUS treatment lesion size

Differences to SWI

HV	Method	ΔAP	ΔML	ΔSI	Δr
1	ANT	-0.3	1.4	1.2	1.8
	3T DTI	0.4	0.4	0.3	0.7
2	ANT	0.5	2.8	1.3	3.1
	3T DTI	1.3	1.7	1.1	2.4
3	ANT	-3.0	-1.1	-0.8	3.3
	3T DTI	-2.1	-0.1	0.0	2.1
average	ANT	-0.9	1.0	0.5	2.8
	3T DTI	-0.1	0.7	0.5	1.7

* where r is diagonal/absolute distance between coordinates

Discussion: clinical practice

- The results support our centre's current clinical practice:
  - Both the 3T anatomical and tractography methods would target VIM-S in all HVs
  - Sonications delivered as sphere of energy and cover larger region than depicted by VIM-A
  - For HV 2 where the VIM-A lies anterior to VIM-S, in clinical practice VIM-S would be sonicated

MRgFUS treatments are tailored to patient response, with subablative, temporary doses delivered

Until the desired clinical response – at which point an ablative dose is delivered.

- Demonstrates the utility of tractography:
  - The proximity of all VIMs to the PT and ML tracts
  - Increase of accuracy of VIM-T target
  - Reduce test sonications
  - Reduce risk of adverse effects
  - More patient specific

Limitations

- Small sample size
  - Consider extending the study to include more HVs
  - Consider Older cohort HVs, more representative of tremor patients

- Reliability of VIM delineation on both 3T and 7T MRI
  - Consider increase number of neuroradiologists delineating
  - Consider inter and intra reproducibility assessment
  - Consider increase number of medical physicists participating

- Reliability of DTI
  - Consider open source software vs. CE marked methods

- Dice coefficient affected by our institution's methodology
  - VIM-T is set to extend 6 mm superiorly from ACPC line
  - VIM-T centre of mass is 3mm above ACPC line
  - VIM-A is 2mm above ACPC
  - VIM-S is always largest volume

Future research

- The results from this preliminary dataset are highly promising

There are lots of avenues to investigate….

Data we have….
- Firstly, we want to expand these results to include the left thalamus of this healthy cohort
- we have also scanned an older cohort of 3 HVs (60-80 yo) and would extend the study to include them (6 VIM comparisons)
- we also acquired 7T DTI and QSM and this is something we want to investigate further (DRT?)

- We have treatment data – clinical protocol includes DTI and post-op MRI shows the lesion

Consider:
- expanding this study to a patient cohort
- best part of VIM to target? *Superior? Inferior? Anterior? Posterior?*

Conclusion

- The results from this study are highly promising and suggest that our institution's currently used 3T anatomical and the proposed tractography based methods for inferring VIM position, result in a treatment that would treat the VIM nucleus
- It suggested that tractography may be a more accurate method for targeting VIM
- Thus, providing reassurance that safe and effective VIM targeting can be performed on current clinical scanners
- There is opportunity to optimise VIM targeting with the aid of ultra high field MRI (7T) and lots more work to be done…

Thanks

Imperial College Healthcare NHS Trust

Imperial College London

FUS Clinical Team

- Prof Wladyslaw Gedroyc (Professor of Radiology)
- Prof Dipankar Nandi (Professor of Neurosurgery)
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- Dr Brynmor Jones (Consultant Neuroradiologist)
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- David Tao (Superintendent Radiographer)
- Michelle Lawrence (Senior Radiographer)
- Susie Wickes (Superintendent Radiographer)

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- Dr Nada Yousif (Biomedical Engineer)
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- Tina Stoycheva (Clinical Research Coordinator)

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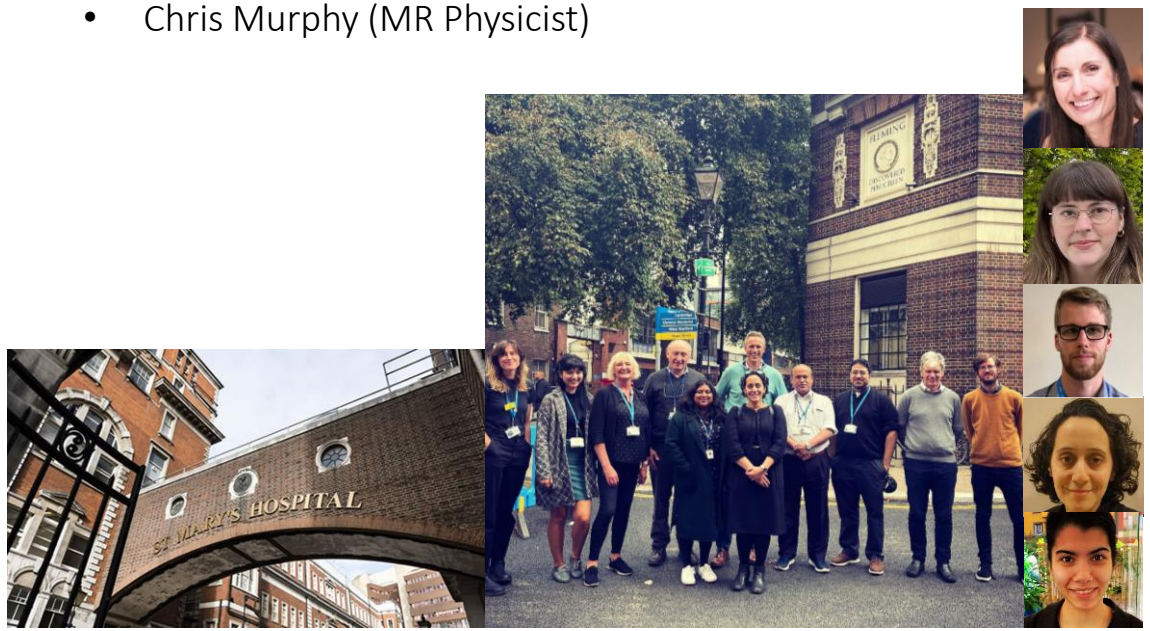
- Dr Mary Finnegan (Principal MR Physicist & MRSE)
- Chris Murphy (MR Physicist)



References

[1] Najdenovska et al., *Comparison of MRI-based automated segmentation methods and functional neurosurgery targeting with direct visualisation of the Ventro-intermediate thalamic nucleus at 7T;* 2019; Sci Rep **9:** 1119.

[2]Krishna et al., *Prospective Tractography-Based Targeting for Improved Safety of Focused Ultrasound Thalamotomy;* 2019; Neurosurgery **84:** 160-168.

[3]Sammartino et al., *Tractography-Based Ventral Untermediate Nucleus Targeting: Novel Methodology and Intraoperative Validation;* 2016; Mov. Disord. **31:** 1217-1225.

Detection of Vestibular Schwannomas in MRI using Convolutional Neural Networks

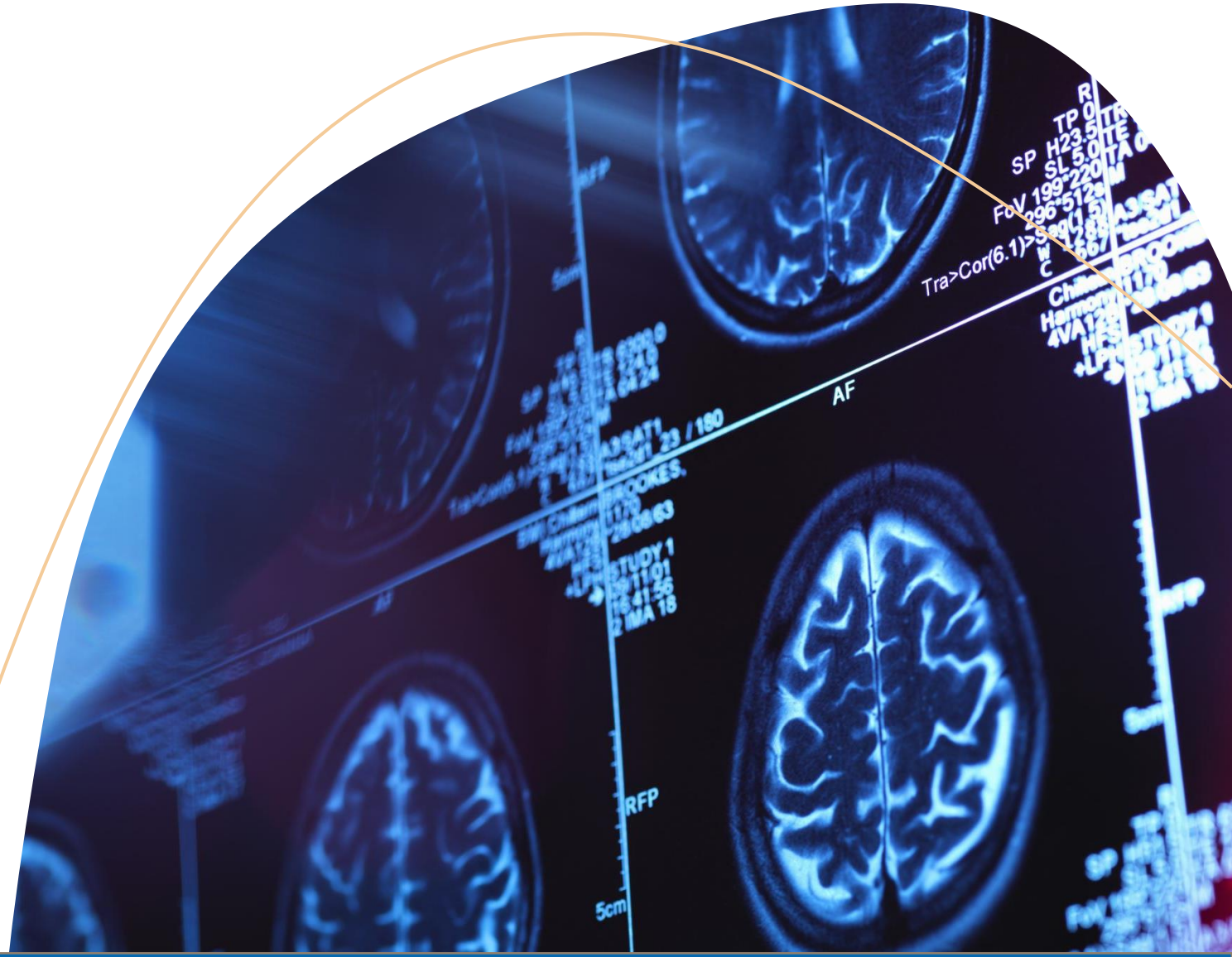
Helen Le Sueur | Scientific Computing | Royal Surrey Hospital NHS Foundation Trust

Collaborators:

Dr Emma Lewis

Dr Matthew Grech-Sollars

Dr Sarah Watson



Introduction

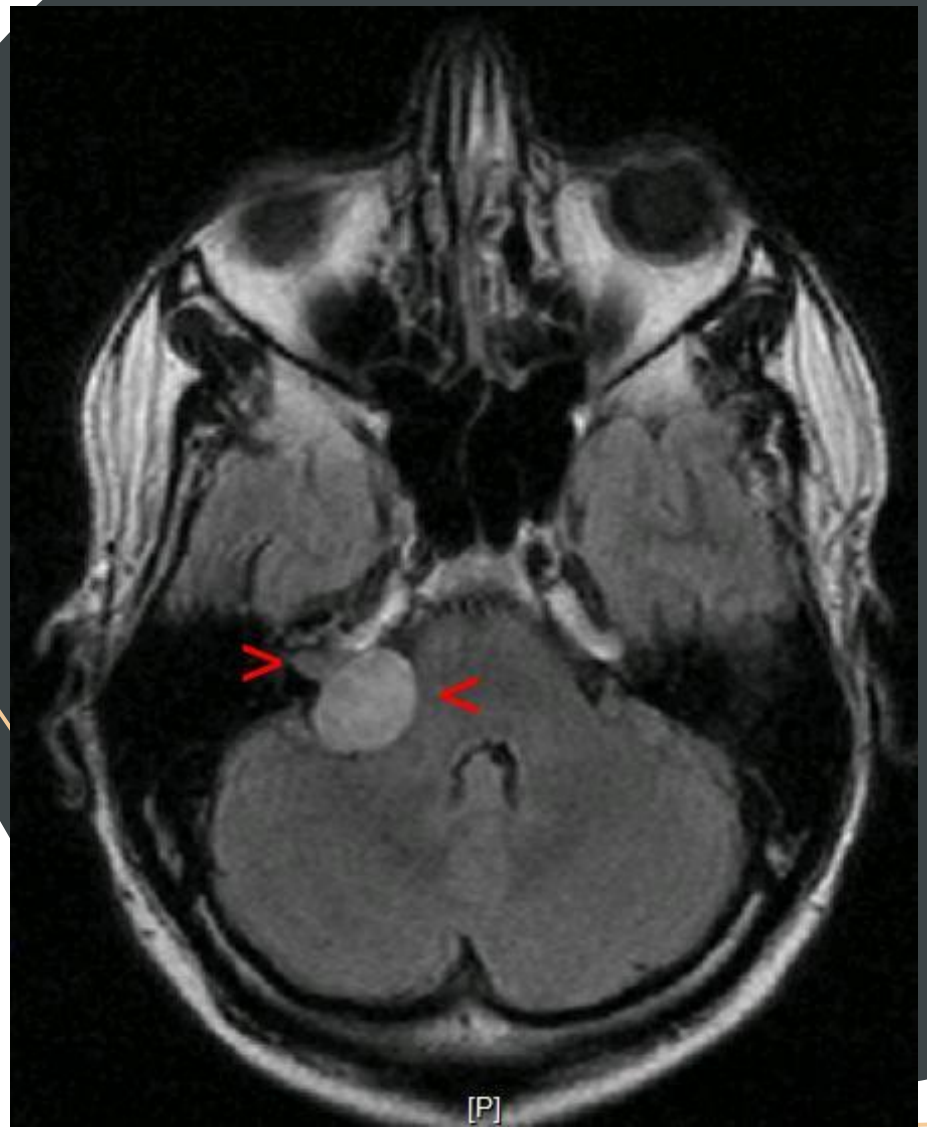
- Large numbers of patients are screened for VS, small percentage (~1%) of those screened have a VS.
- Heavy burden on radiologist's time
- Automatic VS detection could support screening or diagnostic workflows

So…

- What are Vestibular Schwannomas?
- What are the current methods for screening and diagnosis?
- What computational methods can be used?

Introduction: Vestibular Schwannomas

- Small, non-cancerous brain tumour
- 8% of all intracranial tumours are VS
- Commonly arising from vestibular portion of vestibulocochlear nerve (CNVIII) in the IAC (internal auditory canal)
- Early symptoms: hearing loss, dizziness, tinnitus
- Later symptoms: facial numbness, weakness or paralysis, rarely: obstructive hydrocephalus

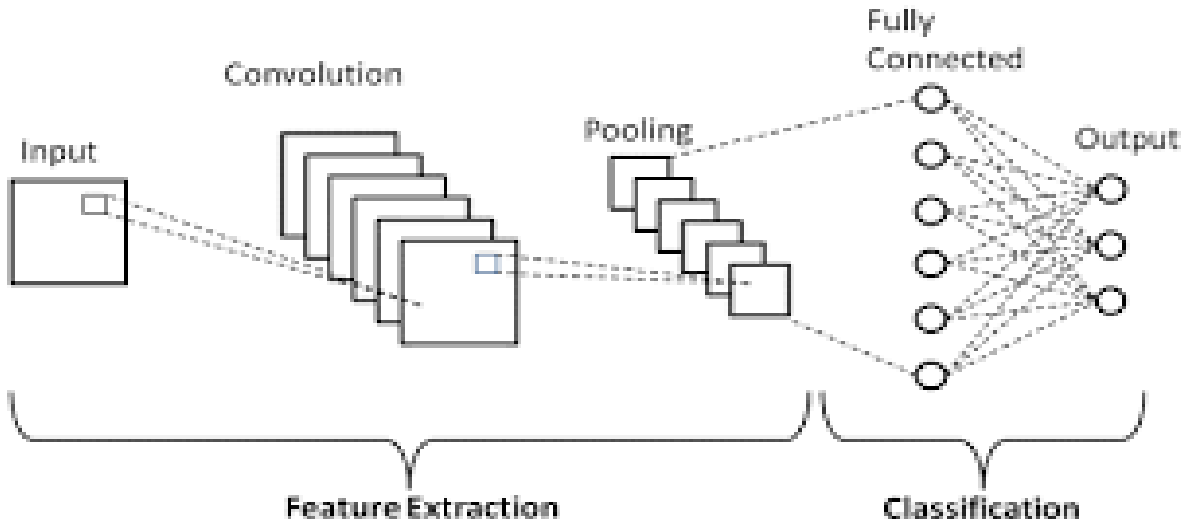


Introduction: Current screening and diagnostic practices

- **Audiometry**, **vestibular function** tests
- **Imaging** – tumours are small, but confined to the internal auditory canal (IAC) – high resolution MRI imaging of this area is the main screening and diagnostic approach
- Dedicated IAMS (internal acoustic meatus) protocol: e.g. T2 TSE, T2 SPACE, FIESTA, FIESTA-C

Introduction: Computational methods

- Learning algorithms: An algorithm where the precise instructions are not known - they are ‘learnt’ via some feedback method such as reinforcement
- Convolutional neural networks: A special type of artificial neural network for visual data such as images



Aims

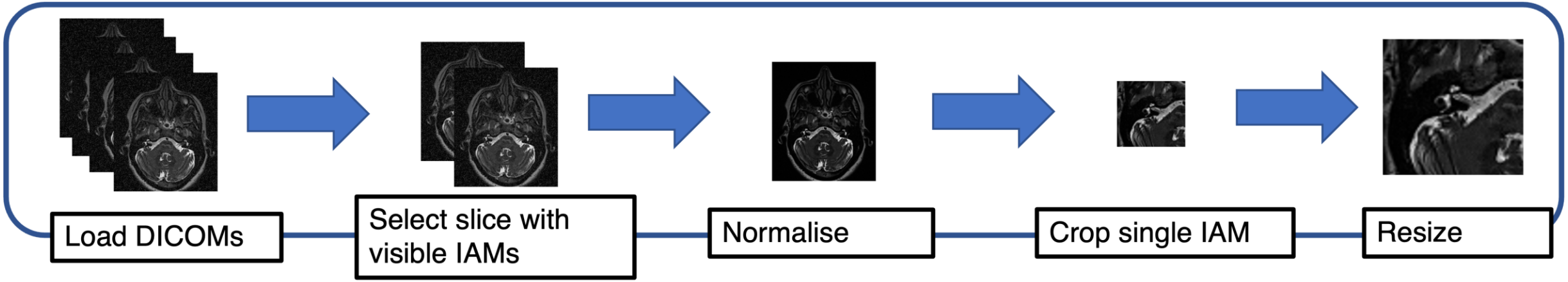
- To add to the growing body of work demonstrating that artificial intelligence has a place in tumour detection
- To demonstrate the successful automatic detection of VS in MRI images

Considerations

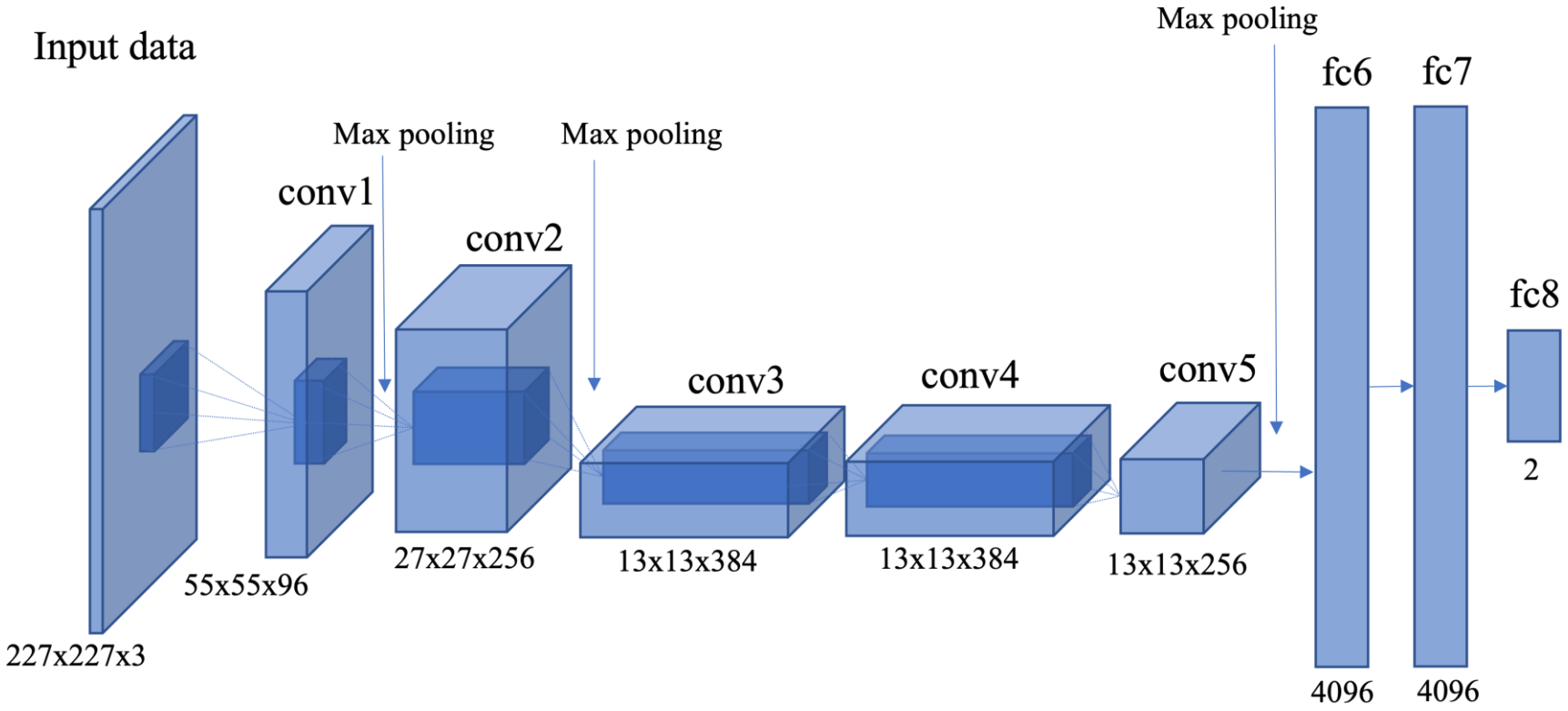
Methods: Data

- Information on 4647 studies was collected from the hospital RIS, using a query to find patients scanned with a dedicated IAMS protocol
- Manually labelled according to the radiologist's report text for:
  - VS negative
  - New VS positive
  - Follow up VS positive
  - Unknown/excluded
- Result: 426 patients (213 pos, 213 neg)
- Hospital PACs queried for all accession numbers associated with those patients.
- All studies were then anonymised and stored

Methods: Image selection and pre-processing



Methods: AlexNet

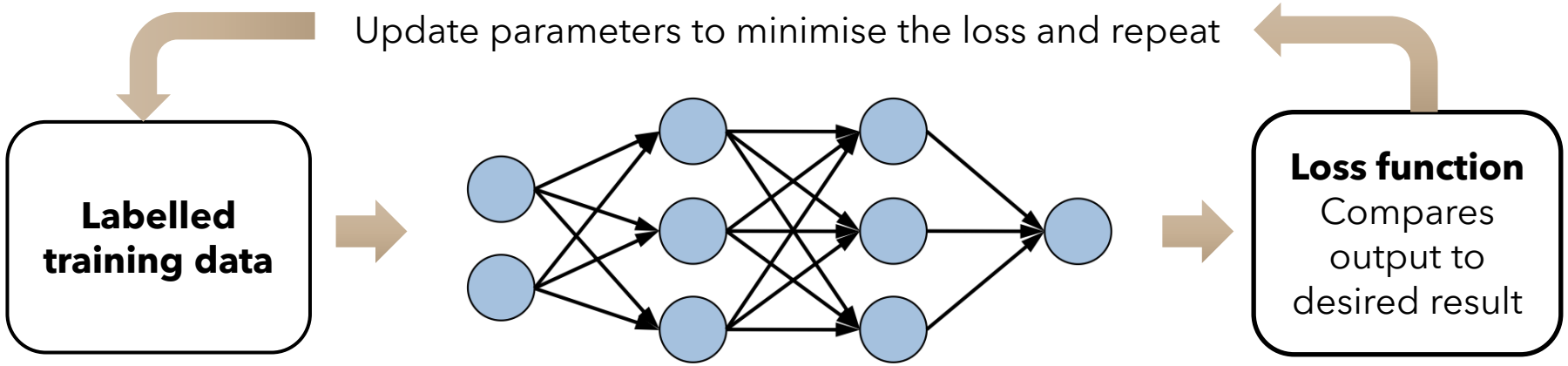


AlexNet: Krizhevsky, Alex, Ilya Sutskever, and Geoffrey E Hinton (2012).

Tumour detection: Khawaldeh, Saed et al. (2017), Abd-Ellah, Mahmoud Khaled et al. (2018).

Model training

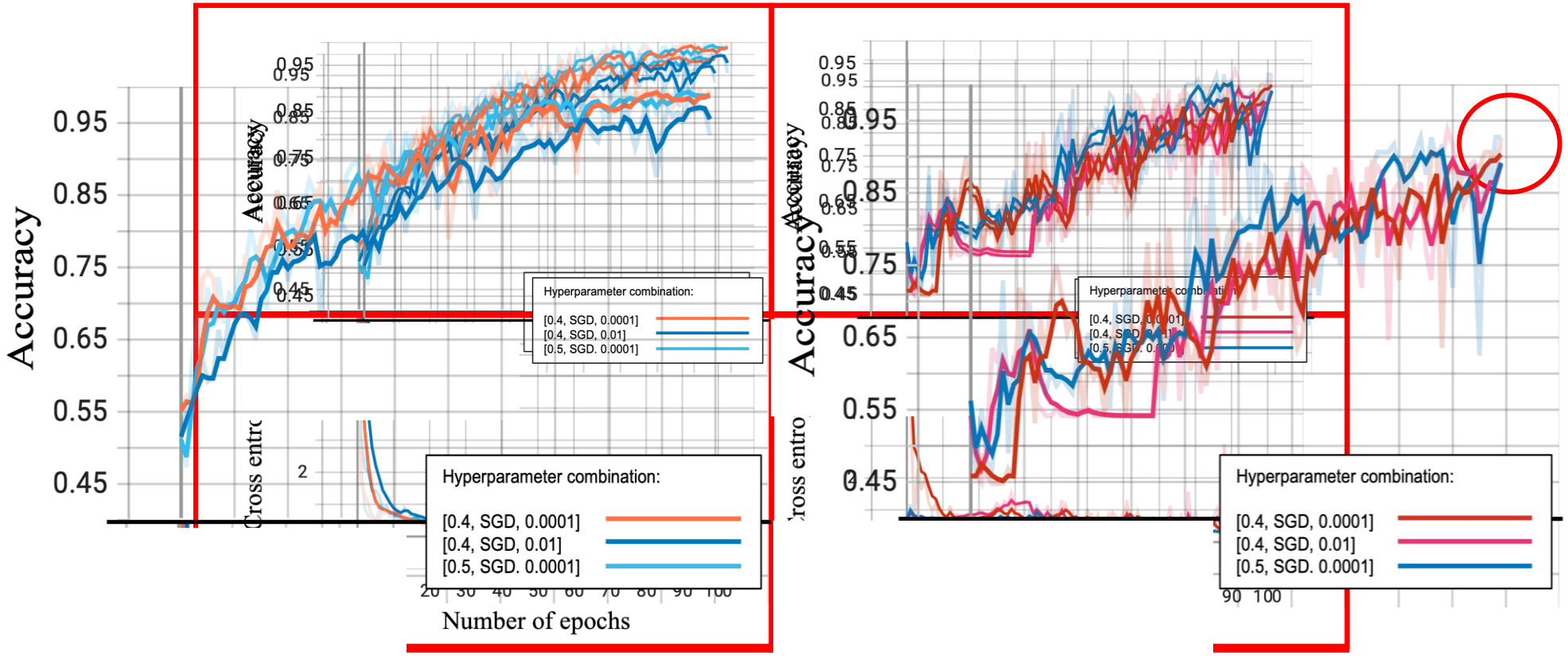
- Training a neural network is the process of finding the appropriate weights for the nodes in the network.
- Labelled images are provided to the algorithm. The resulting output label is compared to the actual label and the network parameters are adjusted iteratively in a direction so that the output gets closer to the desired result



Hyperparameter optimisation

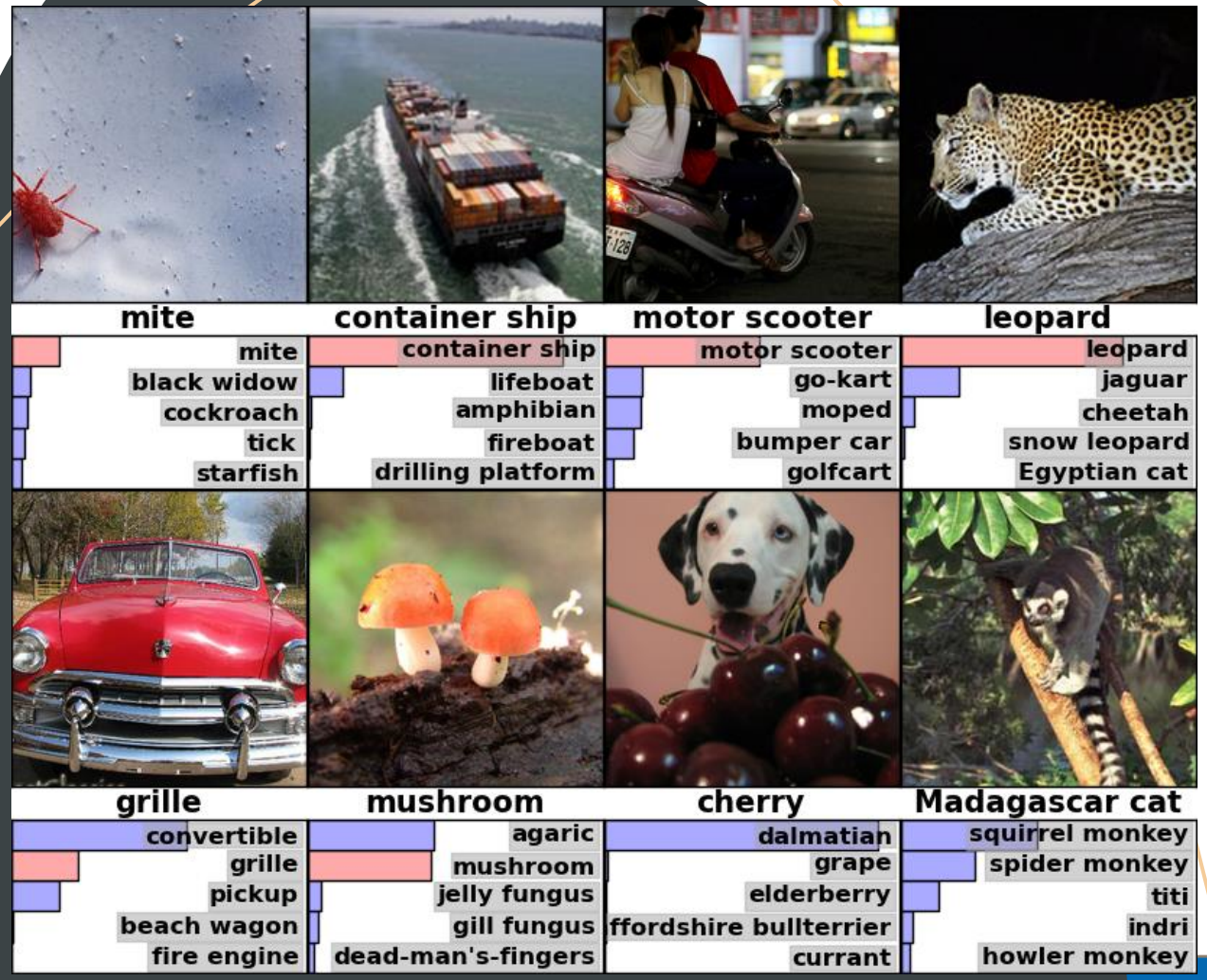
- Choosing the correct hyperparameter values improves the performance of a neural network.
- Hyperparameter optimization involves repeating the training process over different combinations of hyperparameters
- Grid search – all possible combinations of the given hyperparameter space

Results: Hyperparameter optimisation



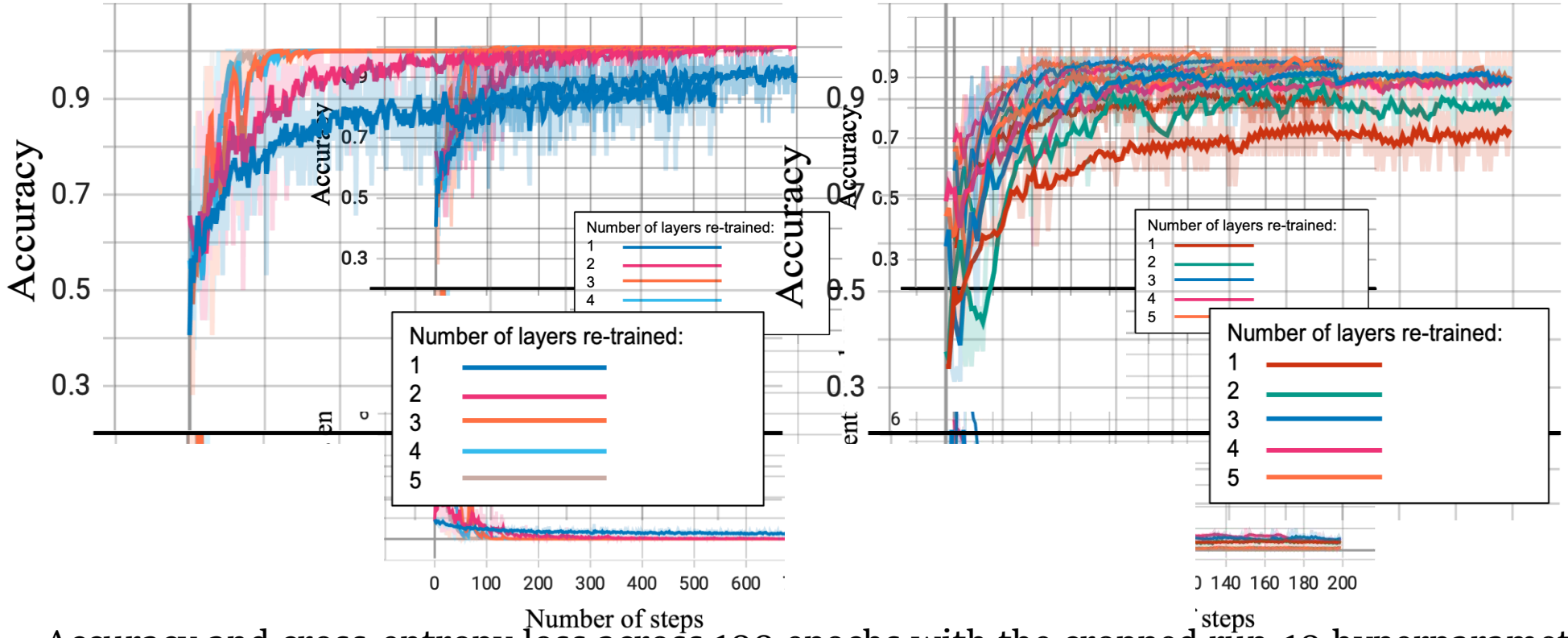
Accuracy and cross-entropy loss across 100 epochs for the top three hyperparameter runs on cropped image patches. The legend shows the hyperparameter values for dropout, optimiser and learning rate for each run.

Transfer learning



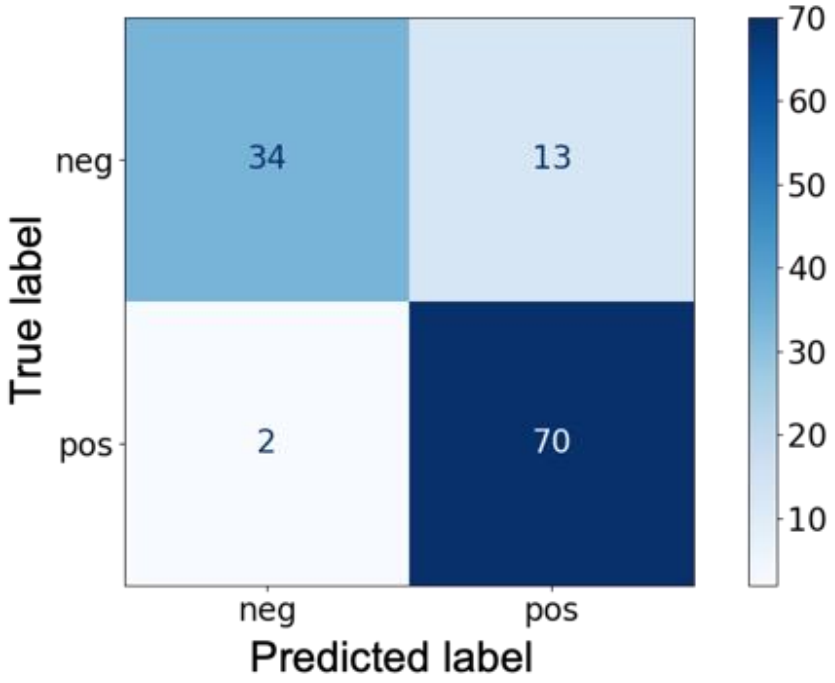
- Transfer learning is where the weights of an already trained model are transferred to be used with a new data set
- ImageNet dataset – pros and cons
- Does transfer learning improve the accuracy?
- Used the 3 best combinations of hyperparameters from the optimization stage

Results: Transfer learning

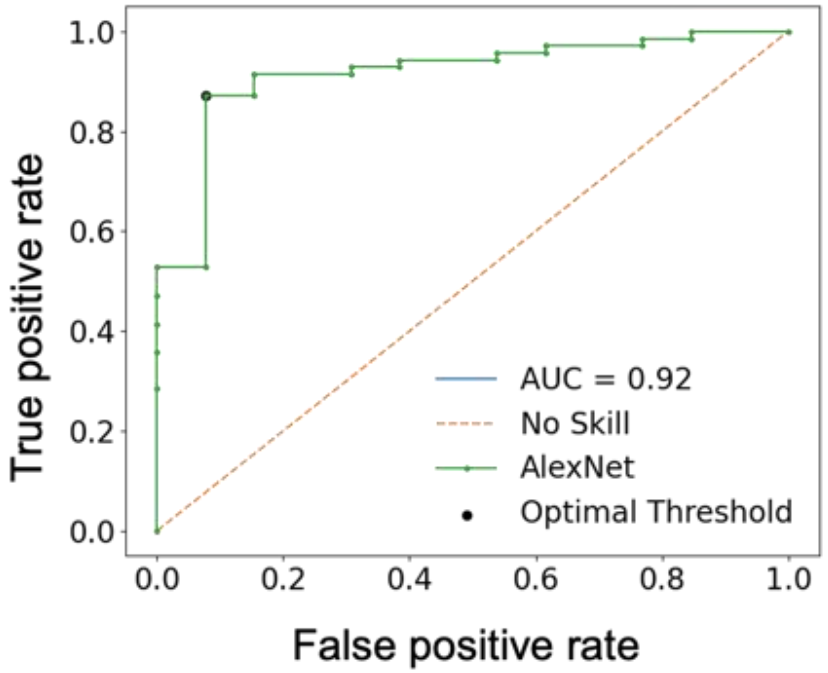


Accuracy and cross-entropy loss across 100 epochs with the cropped run-10 hyperparameters.
Each line represents a training/validation run with the top n layers of the model re-trained.
Total steps = number of epochs*batches per epoch

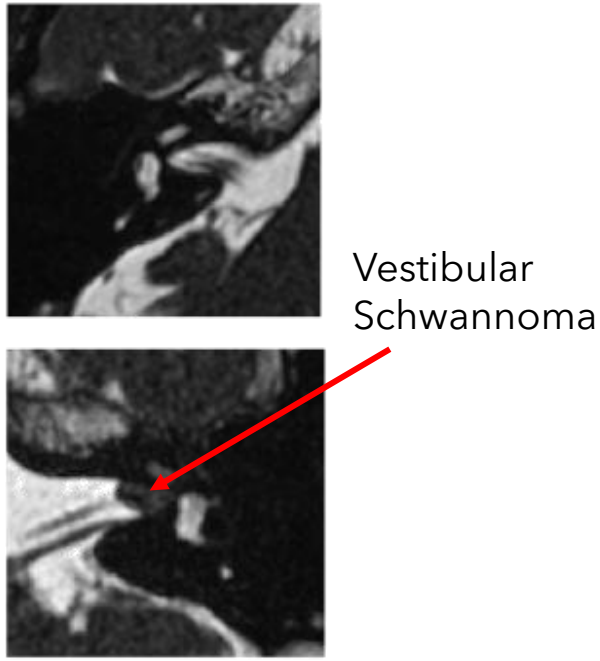
Results: Evaluation



(a) Confusion matrix



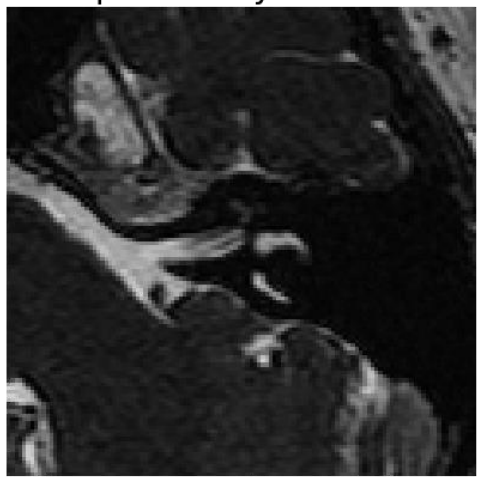
(b) ROC curve



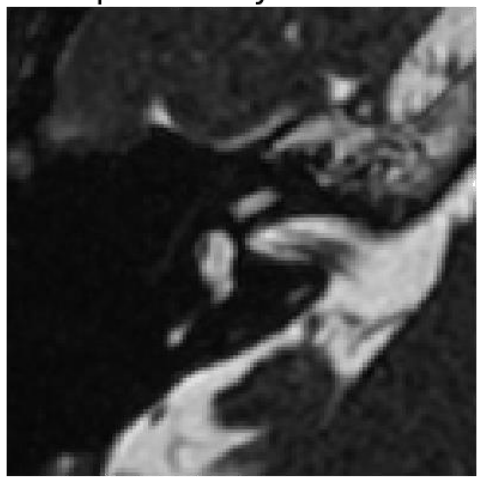
(c) Example of a negative (top) and positive (bottom) image patch

Results: Examples

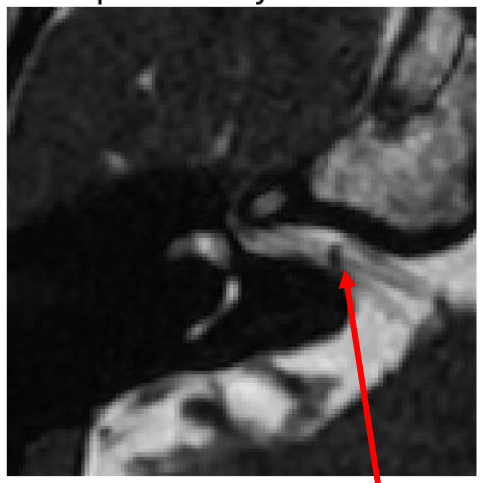
True/predicted class: neg/pos
probability: 0.652



True/predicted class: neg/neg
probability: 0.984

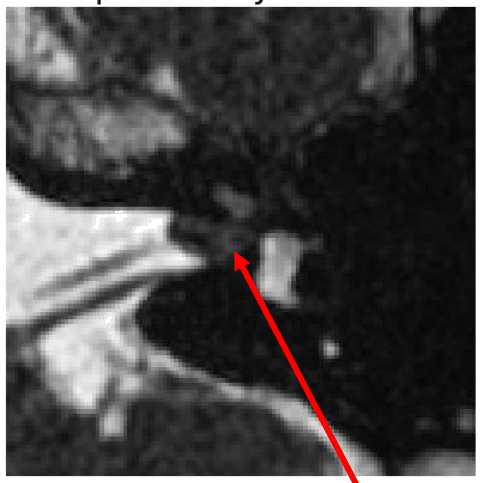


True/predicted class: neg/pos
probability: 0.924



Query
Vestibular
Schwannoma

True/predicted class: pos/pos
probability: 0.921



Vestibular
Schwannoma

Conclusions and future work

- Positive first step towards implementing automatic VS detection as part of a clinical screening workflow
- Next steps:
    1. Improve model
    2. Collect more data
    3. Validate model
    4. Plan integration into clinical practice

Thank you for listening!

Clinical Translation in the Advanced Neuroimaging Facilities in Scotland

IPEM MR-SIG Advanced NeuroImaging – from research to clinical implementation

Birmingham 15/11/22

Dr J Macfarlane, NHS Tayside & SINAPSE Director.

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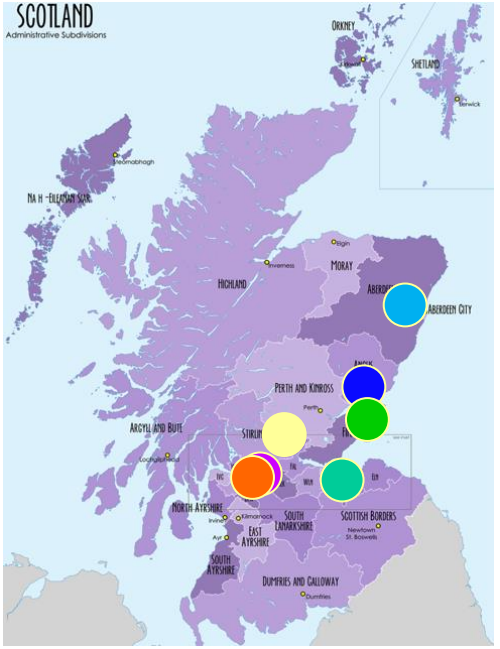
Scottish Imaging Network:
A Platform for Scientific Excellence

SINAPSE

University of Aberdeen · University of Dundee · The University of Edinburgh · University of Glasgow · University of St Andrews · University of Stirling · University of Strathclyde Glasgow · Scottish Funding Council (Promoting further and higher education) · Chief Scientist Office

Scotland-wide initiative for medical imaging research, education and knowledge exchange, funded from 2007

Supported by strategic investment from Scottish Funding Council, with institutional contributions from partner Universities and Chief Scientist Office of NHS Scotland



Who is the SINAPSE pool?

SINAPSE

SINAPSE is only pool supported by CSO/NHS

Researchers who use/develop human imaging techniques

- MRI, CT, PET, SPECT, EEG, MEG, ultrasound, retinal imaging…

Disciplines represented:

- medical physics, chemistry, psychology, computing science, biomedical engineering…
- Medicine (Radiology, Stroke medicine, Psychiatry, Cardiology, Respiratory medicine)

Built on strong foundations

- NHS
- Academia
- Industry facing partners

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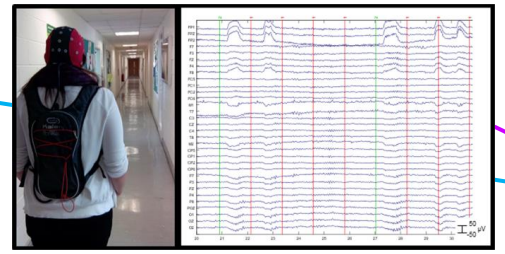
Imaging facilities

FFC-MRI at Aberdeen

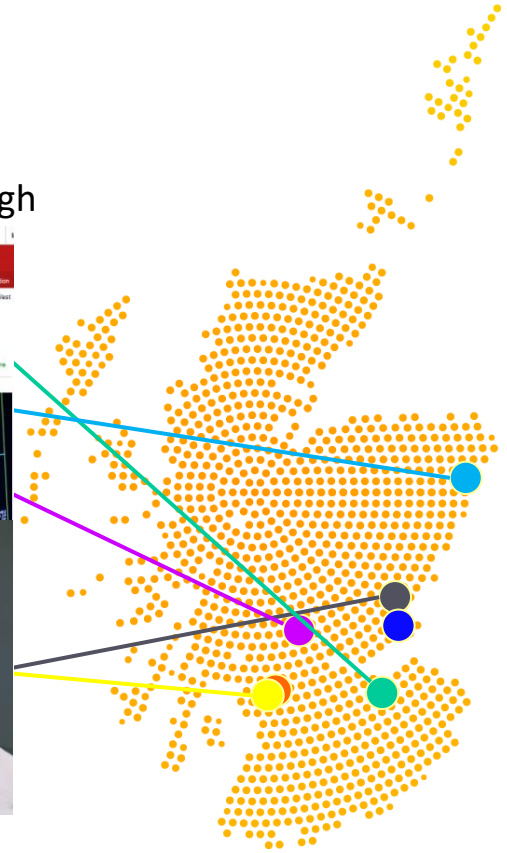


Mobile EEG at Stirling

MR-PET at Edinburgh

7T MRI at Glasgow

MRgFUS in Dundee



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A Platform for Scientific Excellence

University of Aberdeen · University of Dundee · The University of Edinburgh · University of Glasgow · University of St Andrews · University of Stirling · University of Strathclyde Glasgow · Scottish Funding Council · Chief Scientist Office

Fast Field Cycling in Aberdeen

Field Cycling imaging

- Low magnetic field strength -

(0.2 mT – 0.2 T)

- Field is switched rapidly during scan
- T1 evolution with B_0

Neuroimaging applications/ research interest

- Characterisation of ischaemic stroke

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Fast Field Cycling in Aberdeen

- Close working relationship between NHS Grampian and Uni of Aberdeen.
- Significant investment
- Commissioning of new FFC scanner, magnet delivery 2022.
- Adjacent to current 3T scanner
- 10cm wider bore (current model 50cm)
- Commercial collaboration
  - Tesla Engineering, Performance Controls Inc., WideBlue Product Design and Development, Futura Composites, RS2D

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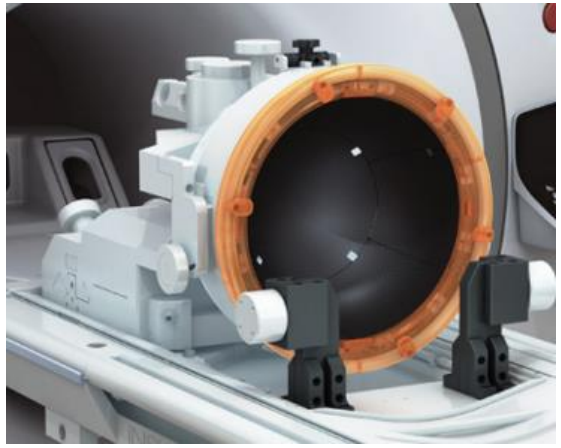
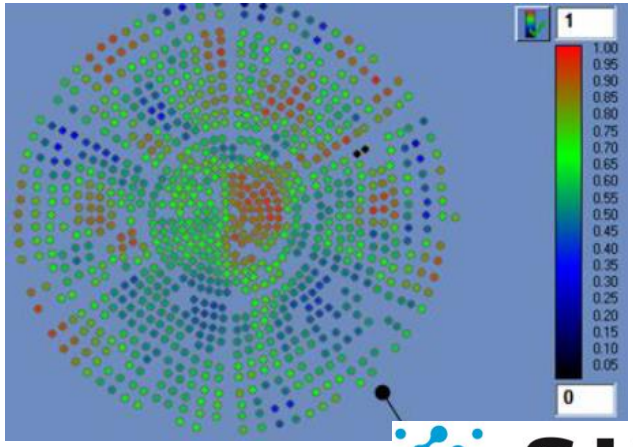
MRgFUS in Dundee



INSIGHTEC



- 2nd installation in UK
- Scotland wide NHS recruitment for NICE guideline approved ET treatments
- First treatment June 2021.
- N=23 unilateral treatments completed.
- Starting point has been clinical use.

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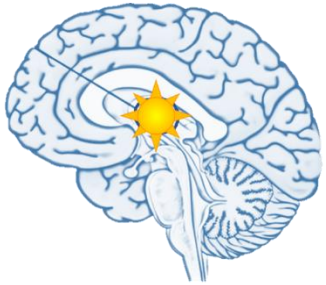
MRgFUS in Dundee

UNIVERSITY OF DUNDEE

Future Research

- Participation in a multicentre Parkinson's study, treating patients with tremor-dominant patients
- Bilateral ET treatments
- Longer term interest in neuromodulation

INSIGHTEC



SUNRISE
Safety and efficacy of thalamotomy by Ultrasound for Parkinson's disease

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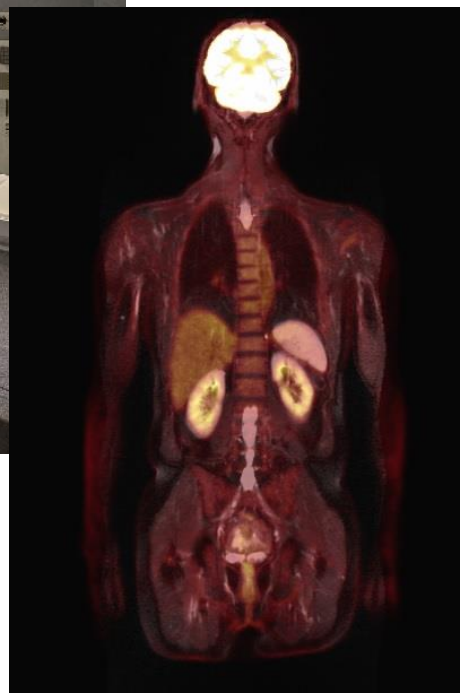
PET/MR in Edinburgh



- Majority of scanning is on a clinical research basis.
- PET-MR is part of the clinical pathway in some cardiac conditions. Lead by Cardiology.
- Research successes in cardiac, vasculitis and brown fat.
- Neuroimaging work towards Alzheimer's phenotyping.
- Radiotracer availability

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7T MRI in Glasgow

University of Glasgow

- Siemens 7T Terra

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7T MRI in Glasgow

University of Glasgow

- Not used in clinical pathways
- Clinical research studies underway
- Coil Development
- Mainly Neuro work:
  - Stroke, epilepsy, oncology, neuroinflammation.
- Industrial collaborations
  - Siemens, MRCoilTech, UoG, NHSGGC, InnoScot, WideBlue

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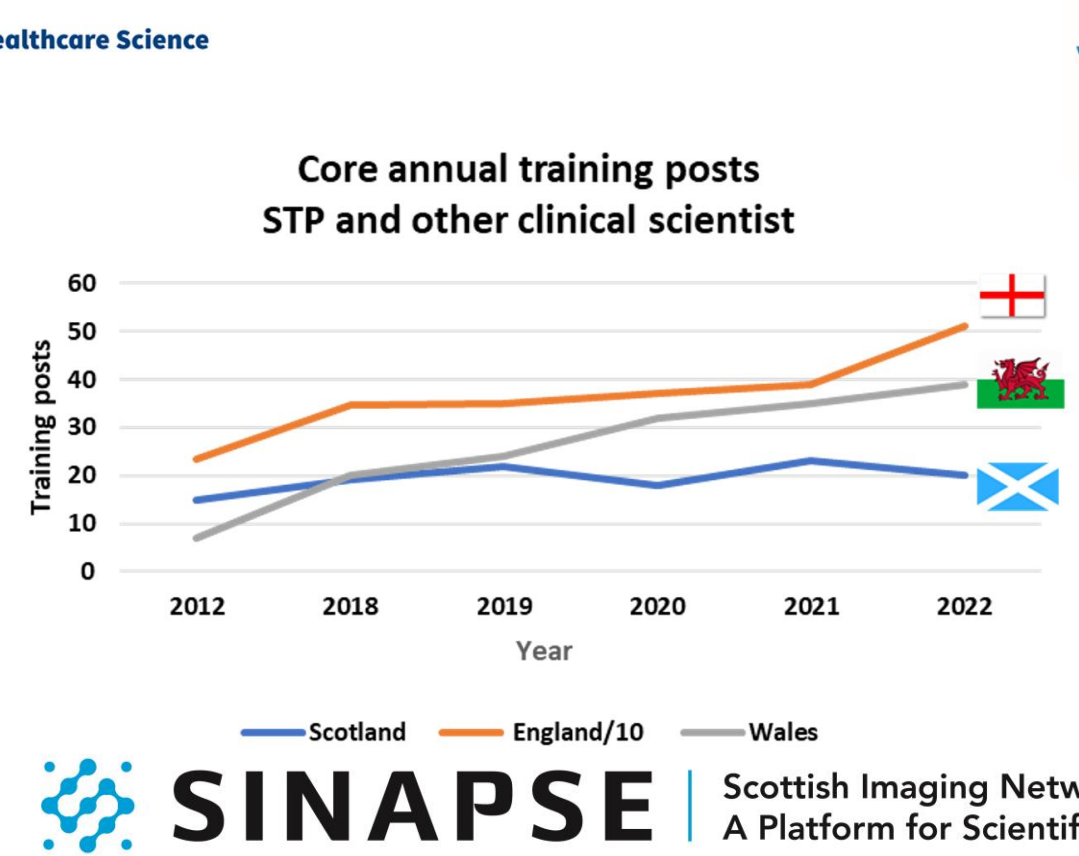
Access to 3rd party sequence developments

- Contracts
- Approach to Risk
- Risk Assessment
- Communication between centres

Training the next generation

- NES (NHS Education for Scotland) has announced a significant reducing training places for all Clinical Scientist including Medical Physics and Biomedical Engineers



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Summary

- Array of cutting edge imaging facilities.
- Capable of advanced neuroimaging applications
- Clinical research performed widely
- Full translation into clinical practice is a work in progress.
  - Challenges:
    - Institutional acceptance of risk
    - Communication with clinical colleagues
    - Scanner time/availability
    - Staffing
  - Routes to success?
    - Greater commercial/industrial collaboration
    - Greater co-operation, networking and cross-disciplinary engagement

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- Kristin Flegal
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- Lucy Kershaw
- James Ross
- Tom Gilbertson

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Introduction of a Novel, Convenient ADC Phantom for Multicentre Routine Quality Assurance of Clinical Diffusion Weighted Imaging Protocols

[1,2]Rebecca Sawbridge, [1,2]Lara Worthington, [1]Zack Ravetz, [1]Roya Jalali, [1]Robert Flintham, [1]Nigel Davies

[1]RRPPS, University Hospitals Birmingham NHS Foundation Trust

[2]Childhood Brain Tumour Research Team, Birmingham Women's and Children's NHS Foundation Trust.

Declarations

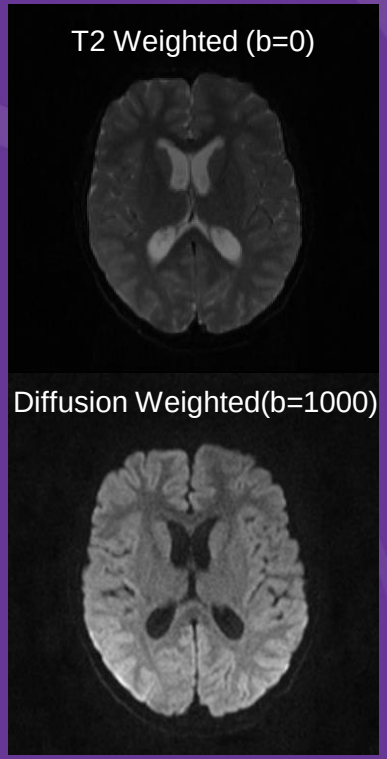
- We have no financial or personal interests to declare regarding the contents of this presentation

Overview

- Background to Diffusion Imaging and ADC measurements
- Overview of QA and Phantom Studies
- Aims and Objectives
- Our Methodology
- Results
- Discussion
- Conclusion and Future Work

Diffusion Imaging

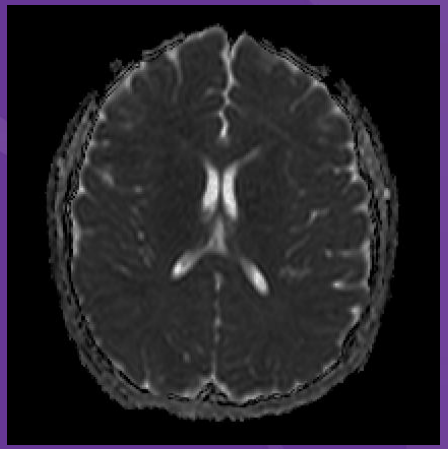
- Diffusion Weighted Imaging (DWI) measures the diffusion/movement of water within the body.
- In diseased tissue free movement of water can be restricted
  - rapid cell division and/or cell swelling – more densely packed cells
- Quantitative measurement of restriction in the diffusion of water can be measured using the Apparent Diffusion Coefficient (ADC)



Apparent Diffusion Coefficient (ADC)

- Quantitative MRI biomarker commonly used in neuro imaging.
  - ADC maps are used to distinguish between normal and diseased tissue e.g. in cancer to diagnose benign vs malignant lesions.
  - Acquire multiple b value images and calculate ADC for each pixel

$$S \propto S_0 e^{-b \times ADC}$$

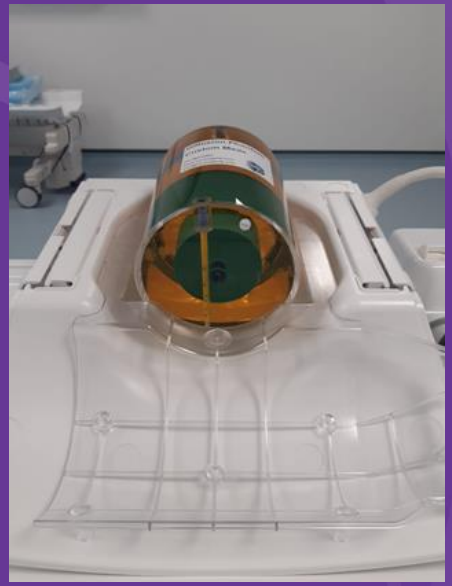


Example Brain ADC map

- Quantitative ADC measurements used to inform clinical decisions
  - Relatively small range of clinically useful ADC values of approx. 0.6-1.6μm^2/ms
  - Low ADC indicates higher malignancy.
  - Identify pre-morphological cancer changes

Multi Centre QA of ADC measurements

- Need to validate ADC measurements across multiple centres.
- Can use phantoms or volunteers (1)
- Need standardized phantoms
- Designed to contain materials with known temperature dependant ADC values
- Acquire ADC maps with clinical protocols.
- Compare calculated and expected values.



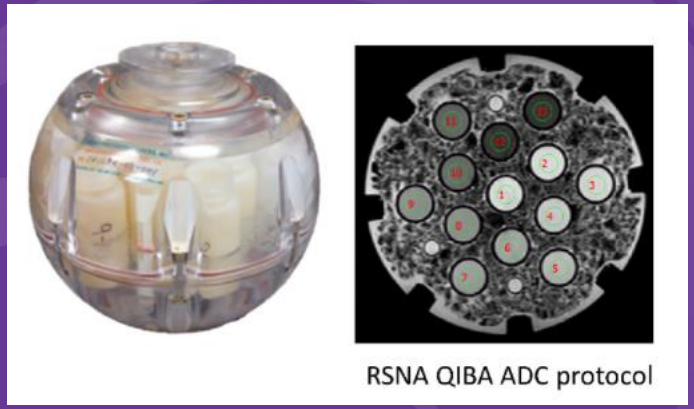
Custom ADC Phantom

(1) Grech-Sollars et al. Multi-centre reproducibility of diffusion MRI parameters for clinical sequences in the brain. NMR Biomed. 2015

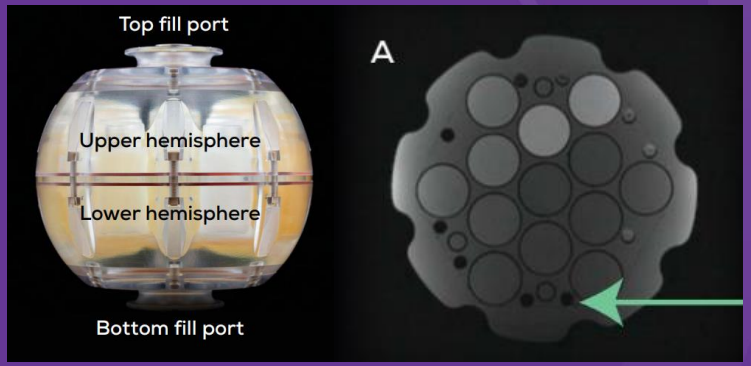
Current Standards

1. Ice-water phantom design
    - e.g. RSNA/NIST phantom (2,3)
    - Account for temperature sensitivity of ADC
    - Disadvantages include:
        - Requires preparation and equilibrium time
        - Access to Ice and Water - impractical

2. MR readable LC thermometer design
    - Caliber MRI diffusion phantom (QMRI.com)
    - NIST Traceable
    - ADC measurements between 15-24ºC
    - New design



NIST QIBA phantom NIST.gov



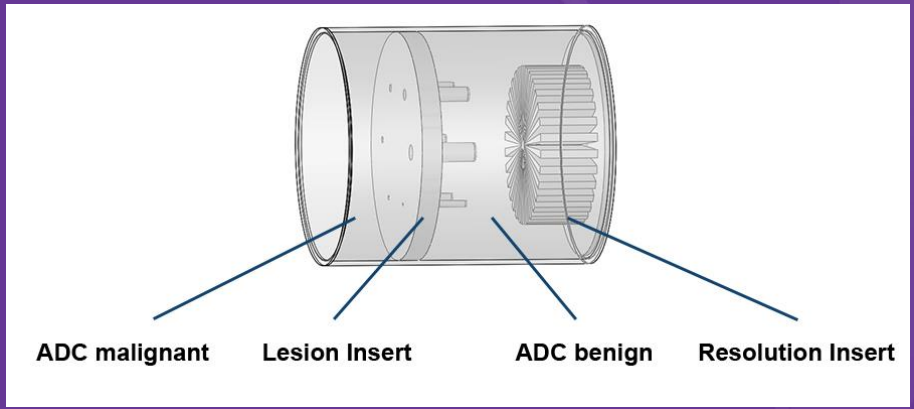
Caliber MRI phantom QMRI.com

(2) Chenevert TL et al., J Magn Reson Imaging. 2011
(3) Malyarenko D, et al.. J Magn Reson Imaging. 2013

HQ Imaging ADC Phantom

- A novel polyvinylpyrrolidone (PVP) based phantom with effective temperature correction has been developed by HQ Imaging (hq-imaging.com/dwi-phantom)

HQ IMAGING
precision in radiology



(4) Wagner F et al., PLoS ONE 2017;12(6): e0179276. https://doi.org/10.1371/journal.pone.0179276

Aims and Objectives

- The aim of this study was to assess the suitability of a new novel custom temperature-calibrated ADC phantom with multiple inserts for routine QA of DWI across multiple clinical sites and scanners.

Methodology: HQ Imaging Phantom Design 1

- 2 main compartments
  - ADC value at 20°C 1.0μm²/ms
  - ADC value at 20°C 1.5μm²/ms
- Temperature correction provided by

$$ADC_{20°C} = \frac{ADC_{measured}}{exp\left(c \times \left(T_{measured} - 20°C\right)\right)}$$

c = 0.0285 1/°C for ADC(20°C) ~ 1.0μm²/ms
c = 0.02453 1/°C for ADC(20°C) ~ 1.5μm²/ms

Issue with internal thermometer which stopped working therefore new customised design introduced

(4) Wagner F et al., PLoS ONE 2017;12(6): e0179276. https://doi.org/10.1371/journal.pone.0179276

Methodology: HQ Imaging Phantom Design 2

- 2 main compartments containing different concentrations of polyvinylpyrrolidone (PVP)
  - (A) ADC value at 20°C 1.0μm²/ms — c = 0.0287 1/°C for ADC(20°C)
  - (B) ADC value at 20°C 1.6μm²/ms — c = 0.0261 1/°C for ADC(20°C)

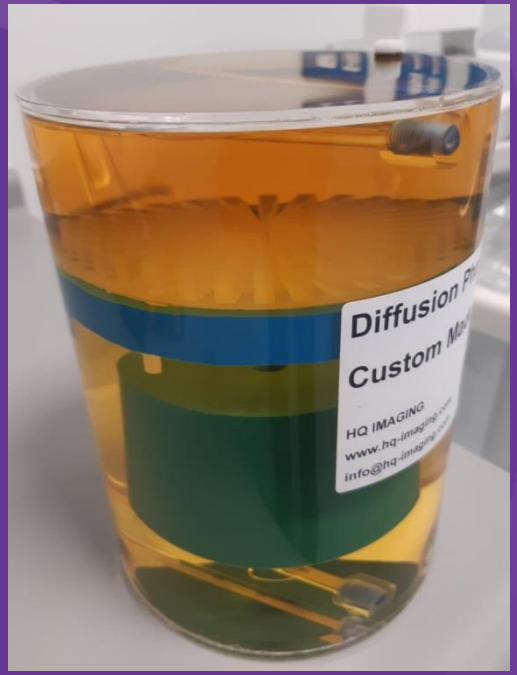
- 4 additional inserts containing different concentrations of PVP
  - (C) ADC value at 20°C 0.6μm²/ms — c = 0.0309 1/°C for ADC(20°C)
  - (D) ADC value at 20°C 1.0μm²/ms — c = 0.0287 1/°C for ADC(20°C)
  - (E) ADC value at 20°C 1.4μm²/ms — c = 0.0269 1/°C for ADC(20°C)
  - (F) ADC value at 20°C 2.0μm²/ms — c = 0.0244 1/°C for ADC(20°C)

- Two internal thermometers
- Resolution and lesion inserts

$$ADC_{20°C} = \frac{ADC_{measured}}{exp\left(c \times (T_{measured} - 20°C)\right)}$$

(4) Wagner F et al., PLoS ONE 2017;12(6): e0179276. https://doi.org/10.1371/journal.pone.0179276

HQ Imaging Custom Phantom Design 2



Methodology

- ADC maps were collected from 6 different models of MRI scanners across 5 sites
  - Siemens Skyra 3T
  - Siemens Verio 3T
  - Siemens Aera 1.5T
  - Philips Ambition 1.5T x2
  - Philips Elition 3T
  - Philips Ingenia 3T
- Total of 28 routine clinical DWI protocols.

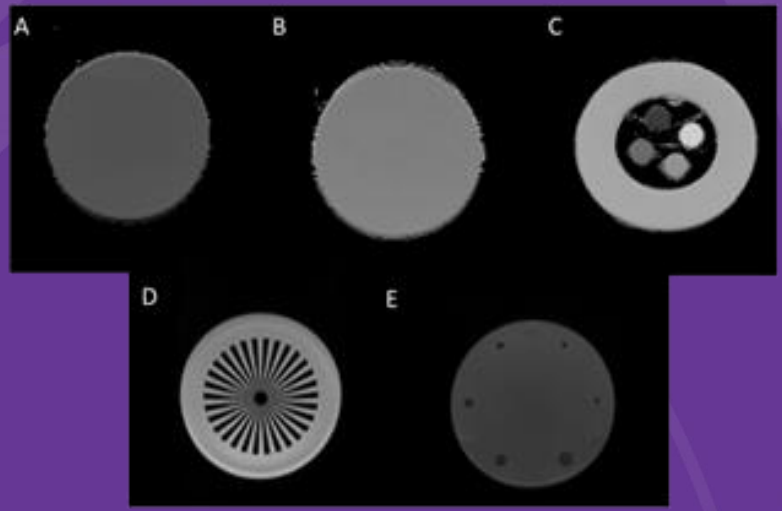
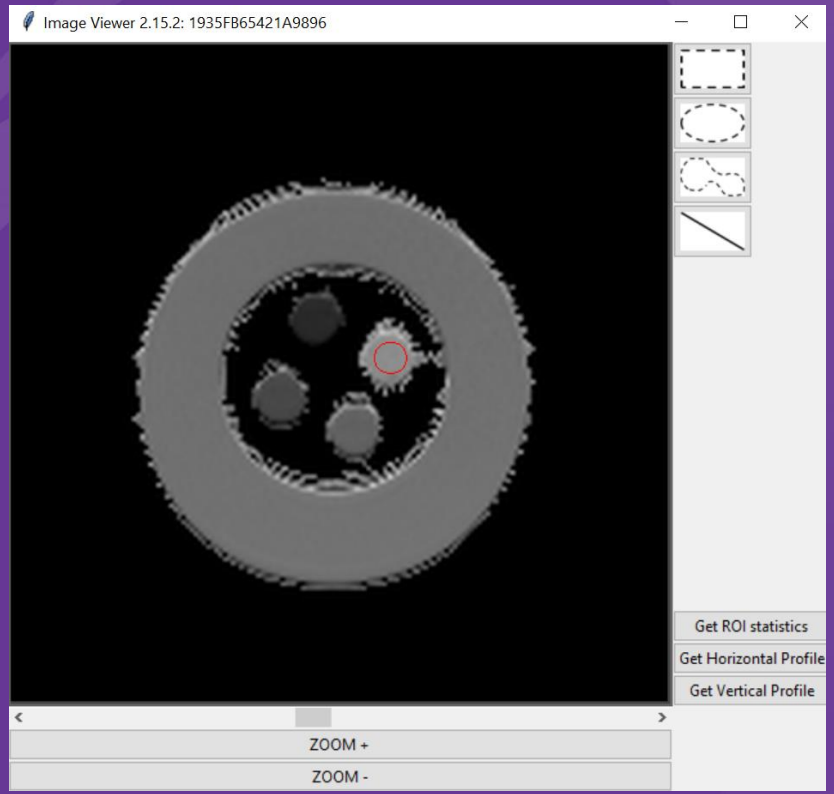


Figure 1. ADC maps of (A) compartment A (B) Compartment B (C) compartments C-F, (D) b0 image of resolution insert, (E) and b1000 image of lesion insert.

ADC measurement

- Phantom temperature was measured before and after each scan
  - Hand held Infra-red thermometer for phantom design 1
  - Internal thermometer readings for phantom design 2
  - Temperature probes are calibrated against a traceable standard

- Manually drawn ROIs
- Temperature corrected ADC mean and standard deviation values calculated:
  - In-house image analysis software “MIPPY”
- Compared against expected values and across scanners and protocols.



Results –Phantom Design 2 validation

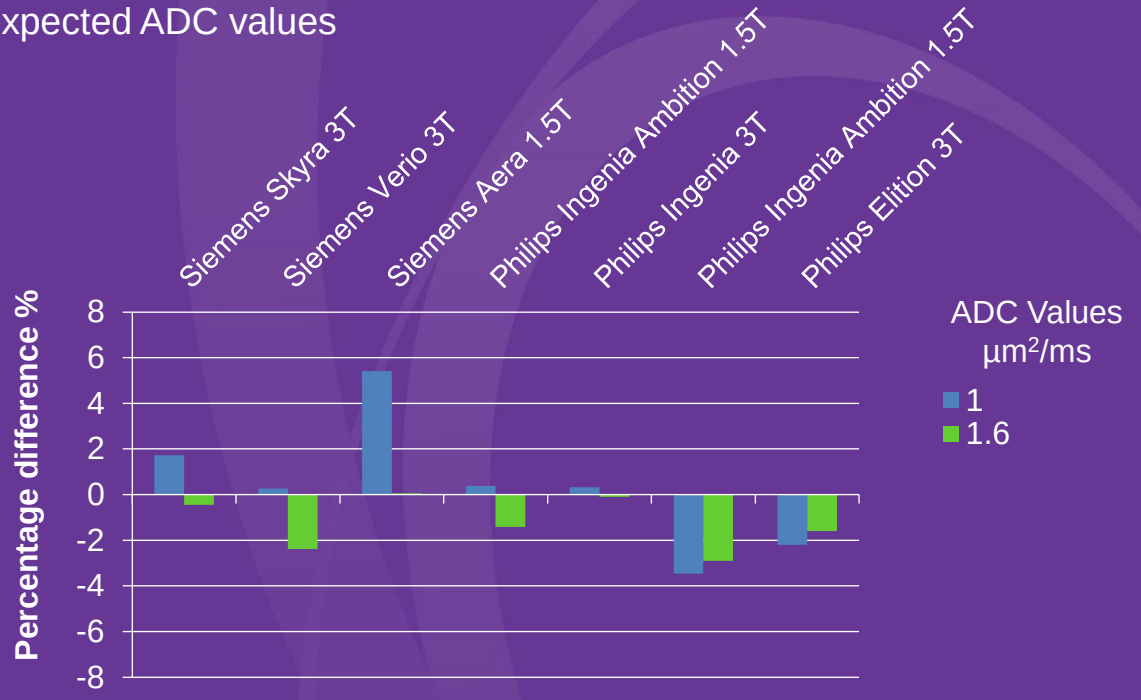
- Comparison between Compartment A with ADC value 1.0μm^2/ms for both Design 1 and Design 2 for 3 hospital sites
- Temperature both measured with handheld infra-red thermometer

%difference between calculated and expected ADC values				
Phantom	Hospital 1 Siemens Skyra 3T	Hospital 1 Siemens Verio 3T	Hospital 2 Siemens Aera 1.5T	Hospital 3 Philips Ingenia Ambition 1.5T
OLD	-2	0	3	0
New	3	-1	5	0

- Comparable results found within +- 5% of expected ADC

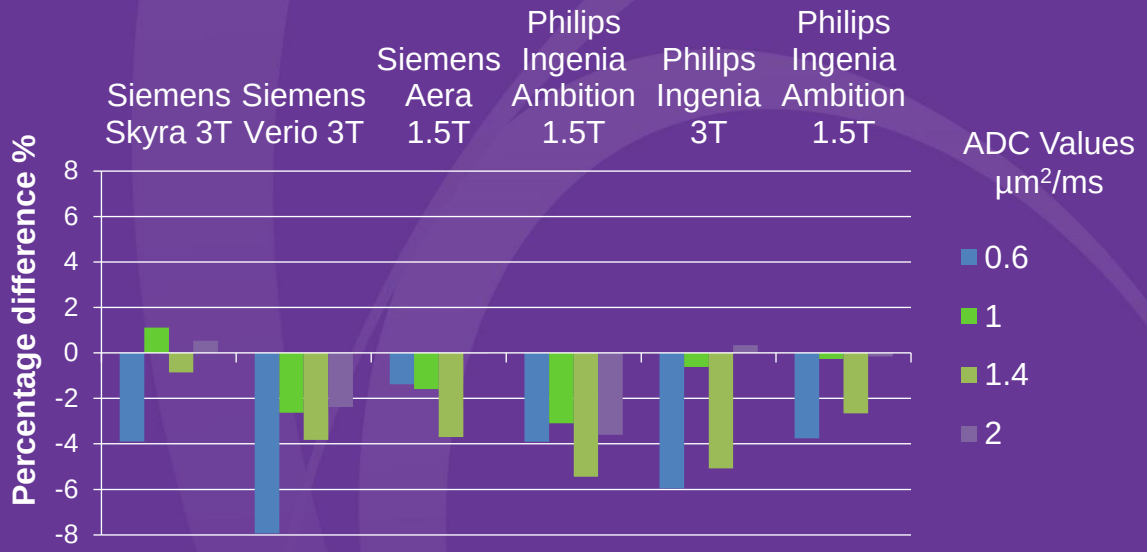
Results- Phantom Design 2 Main Compartments

- Comparison of Compartment A with ADC value 1.0μm^2/ms and Compartment B with ADC value 1.6μm^2/ms against expected ADC values



All Values are within +-5.5% of expected values

Results- Phantom Design 2 Inserts C-F



- Lowest ADC compartment 0.6µm²/ms appears to have greatest variability with largest %diff of -8%
- All other compartments were within +-6% for all clinical protocols.

Discussion

- All calculated ADC measurements were found to be accurate according to the manufacturer's temperature-calibrated values.
- Highest reported variation of -8% in the lowest ADC compartment
- The phantom was simple and quick to use requiring no preparation and short equilibration time
- Provides a convenient and cost-effective method for validating scanner-generated ADC maps across a range of clinical scanners and protocols

Conclusion and Future Work

- A novel ADC phantom has been assessed and shown to provide a convenient and effective method for QA of quantitative DWI protocols in clinical use and multicentre trials.

- Benefits over current ice-water standard
  - Requires shorter equilibrium time
  - Easy to transport to multiple sites
  - Quick and dry! - no ice and water/ preparation required

- Future work includes
  - Gathering more data across more sites and scanner manufacturers.
  - Repeat assessment of the same scanners/protocols to assess repeatability.
  - Utilising the resolution and lesion inserts for further quantitative assessment.

Acknowledgements

- MRI Physics team at University Hospitals Birmingham:
  - Dr Nigel Davies
  - Dr Lara Worthington
  - Dr Roya Jalali
  - Zack Ravetz
  - Robert Flintham
  - Dr Roman Wesolowski
  - Dr Rosa Sanchez Panchuelo

- The continued support from Professor Andrew Peet and the Childhood Brain Tumour Research Team at Birmingham Children's Hospital

Results- Phantom Design 2 Main Compartments

- Comparison of Compartment A with ADC value 1.0μm^2/ms and Compartment B with ADC value 1.6μm^2/ms against expected ADC values

Site	Scanner	Expected ADC μm^2/ms	Average ADC across protocols μm2/ms	%Diff
Hospital 1	Siemens Skyra 3T	1.00	1.02	1.7
		1.60	1.59	-0.4
Hospital 1	Siemens Verio 3T	1.00	1.00	0.3
		1.60	1.56	-2.4
Hospital 2	Siemens Aera 1.5T	1.00	1.05	5.4
		1.60	1.60	0.1
Hospital 3	Philips Ingenia Ambition 1.5T	1.00	1.00	0.4
		1.60	1.58	-1.4
Hospital 4	Philips Ingenia 3T	1.00	1.00	0.3
		1.60	1.6	-0.1
Hospital 5	Philips Ingenia Ambition 1.5T	1.00	0.97	-3.5
		1.60	1.55	-2.9
Hospital 5	Philips Elition 3T	1.00	0.98	-2.2
		1.60	1.58	-1.6

Results- Phantom Design 2 Inserts C-F

Site	Scanner	Expected ADC $\mu m^2/ms$	Average ADC across protocols µm2/ms	%Diff
Hospital 1	Siemens Skyra 3T	0.60	0.58	-3.9
		1.00	1.01	1.1
		1.40	1.39	-0.9
		2.00	2.01	0.5
Hospital 1	Siemens Verio 3T	0.60	0.55	-7.9
		1.00	0.97	-2.6
		1.40	1.35	-3.8
		2.00	1.95	-2.4
Hospital 2	Siemens Aera 1.5T	0.60	0.59	-1.4
		1.00	0.98	-1.6
		1.40	1.35	-3.7
		2.00	2.00	0.0
Hospital 3	Philips Ingenia Ambition 1.5T	0.60	0.58	-3.9
		1.00	0.97	-3.1
		1.40	1.32	-5.4
		2.00	1.93	-3.6

Results- Phantom Design 2 Inserts C-F continued…

Site	Scanner	Expected ADC $\mu m^2/ms$	Average ADC across protocols µm2/ms	%Diff
Hospital 4	Philips Ingenia 3T	0.60	0.56	-6.0
		1.00	0.99	-0.6
		1.40	1.33	-5.1
		2.00	2.01	0.3
Hospital 5	Philips Ingenia Ambition 1.5T	0.60	0.58	-3.8
		1.00	1.00	0.3
		1.40	1.36	-2.7
		2.00	2.00	0.1

Pre-surgical evaluation in epilepsy patients: clinical reliability of the “Home Town Walk” fMRI paradigm for lateralisation of memory function

Nigel Davies[1], Roya Jalali[1], Roman Wesolowski[1], Robert Flintham[1], Rosa Sanchez-Panchuelo, Vijay Sawlani[2]

[1]RRPPS, Medical Physics [2]Radiology,
University Hospitals Birmingham NHS Foundation Trust

Background

- Memory-activated functional MRI (fMRI) is increasingly implemented in the clinic to assess memory function as part of pre-surgical decision making in refractory epilepsy
- The Home Town Walking (HTW) fMRI paradigm has been shown to activate the parahippocampal gyri (PHG) and help determine memory lateralization in epilepsy patients [Janszky J et al., Epilepsia, 2005]
- Limited data are available on the reliability of this technique or its use in clinical practice

Aim

This study aims to assess the robustness of the HTW paradigm for lateralising memory function and aiding surgical planning in a large consecutive series of epilepsy patients in the clinical setting

Methods: Sample

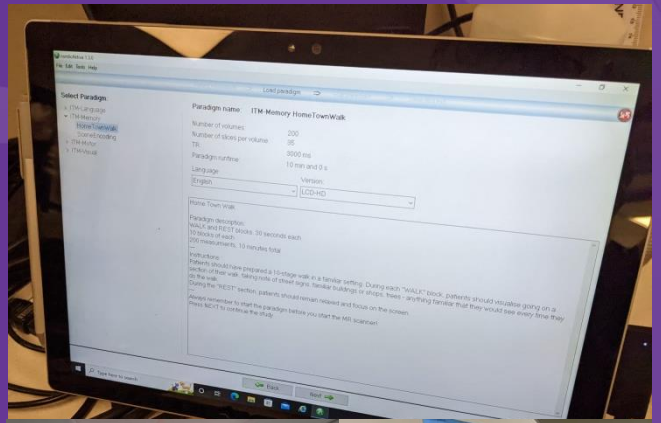
- Patients with refractory Temporal Lobe Epilepsy undergoing assessment for potential surgical intervention at QEHB
- All patients were instructed to prepare a familiar “imagined” walk and were asked to attend two scanning sessions on separate days
- Scans usually <48 hours apart, but <14 days counted as single “episode”
- Consecutive series from Apr 2015 – Apr 2022:
  - ❑ 117 unique epilepsy patients
  - ❑ 246 separate scanning sessions

Methods: Acquisition

- A block-design HTW memory paradigm performed as part of a wider language and memory fMRI assessment (+ high-res 3D T1w, + DTI)
- Patients were scanned across two 3T MRI scanner:
  1. Siemens Verio (2015 – 2018) – QEHB Imaging department
  2. Siemens Skyra (2017 - 2022) – “ITM Imaging Centre”
- BOLD fMRI GE-EPI acquisition:
  - ❑ 3 mm isotropic resolution
  - ❑ TR=2s/3s, [30s “task”, 30s ”rest”] x 10 blocks; Total duration = 10 mins

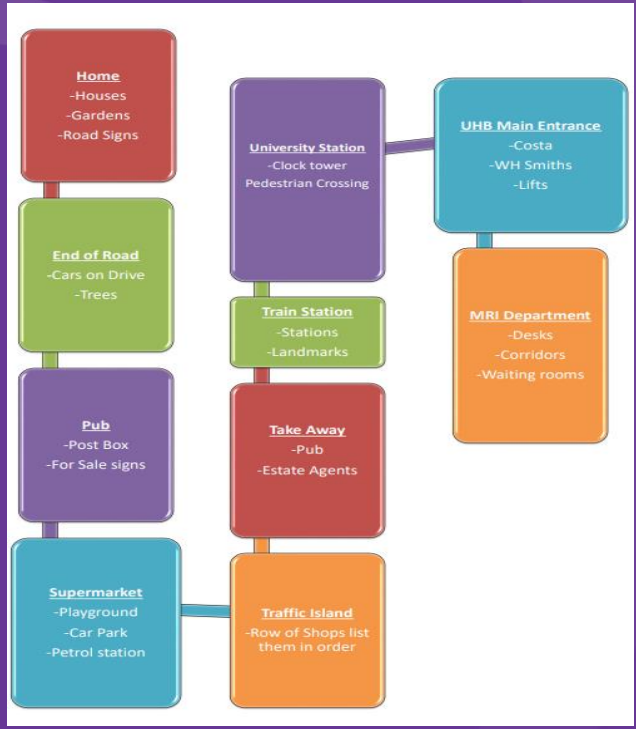
Methods: HTW-fMRI set-up

- Service development led in partnership between radiology and MR physicists
- QEHB Imaging: Standard large-screen monitor displayed through control room window; manual syncing of presentation
- ITM Imaging Centre:
  - ❑ Integrated NNL nordicActiva system
  - ❑ LCD Inroom Viewing Device



Methods: HTW-fMRI Paradigm Design

- Instructions were given to start and end at familiar places, divide the route into 10 blocks and have at least five points for each block.
- During each ‘Walk period’ patients were asked to visualize one section of the walk, focussing on what they can see, hear and smell in as much detail as possible



Methods: HTW-fMRI Patient Preparation

Functional MRI (fMRI) Examination
Memory Walk

Preparation for this scan is critical. If you do not come prepared, we may not be able to perform your scan.
Please ring us if you have difficulties preparing or you require the information in a different format.

This examination is designed to visualise the exact area of your brain which is responsible for your memory.

This information sheet is designed to prepare you for the examination and explain what we require you to do prior to attending for the scan.

Coming prepared for the scan is extremely important and is crucial to the studies success. You will be asked to attend on two days which will be very close together and you must have prepared for the scan on Day 1, having filled in the crib-sheet provided.

We need you to have a short walking journey (about 10 minutes) that you know well, planned in your head, for example, a walk around your local park, or to the local shops. Try and split the journey up into 30 second sections. There is an example over-leaf to demonstrate which shows a walking journey to work. The journey/things you remember must be real.

This part of the examination will take about 10 minutes of continuous scanning. We will ask you to recall your journey or experience in a methodical way and in as much detail as possible. During your scan you will be able to see a screen which will tell you when to 'Walk' and 'Rest'.

During the 'Walk' periods, recount your walk in as much detail as possible. During the 'Rest' periods, remain relaxed and looking at the screen. The 'Walk'/'Rest' periods will alternate for 10 minutes until the scan is complete. If you get to the end of your walk, go back to the beginning and start again. If you lose your place in your walk during the scan, go back to the beginning and start again. If you don't get to the end of your walk, it does not matter.

Plan your 10 minute journey into the 10 methodical blocks and try to have at least five points for each block.

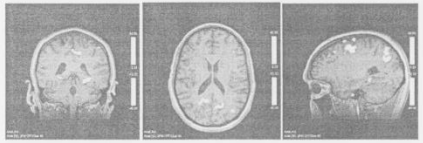
The crib sheet provided is for you to make notes. Whilst this will not be available during the scan, it is important to fill this out in as much detail as possible and practice your journey before you come in for the scan.

This is not a test of your memory, and we will not know what you are thinking.
For the scan to work, it is important that you are accessing real memories in your mind.

It is important whist performing this task that you do it entirely in your head; do not speak the steps out loud. It is also important that you keep your body absolutely still as movement can affect the quality of the scan.

The radiographers will go through these instructions before you start the examination and again before each scan so you can ask about anything you are unsure of.

Below are some examples of the images we will produce, with the bright orange areas being the areas of the brain that are being used.

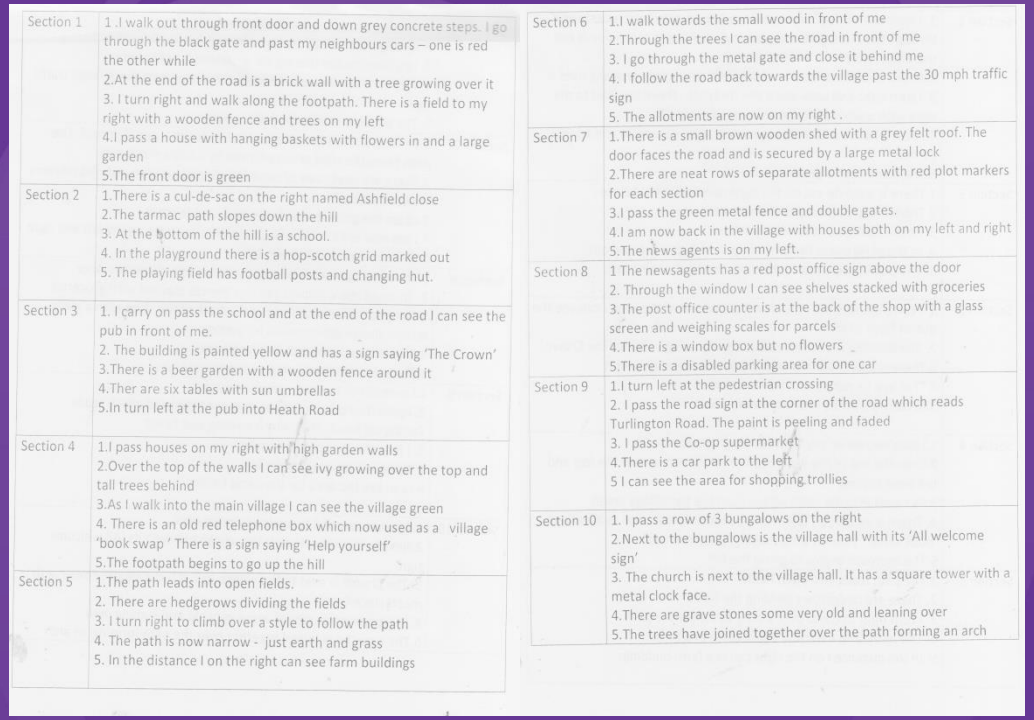


If you have any questions or concerns, please contact:

Jane Herbert – Band 7 MRI Radiographer 0121 371 2233
Eleanor Derrick – Band 7 MRI Radiographer 0121 371 8035

Methods: HTW-fMRI Patient Preparation

"The following is an example of a memory walk divided into 10 sections. Do one for your own walk including at least 5 things for each section. Bring your completed sheet with you on the day of your scan. Practice remembering your walk in your head before your appointment."



Section 1	1 .I walk out through front door and down grey concrete steps. I go through the black gate and past my neighbours cars – one is red the other while 2.At the end of the road is a brick wall with a tree growing over it 3. I turn right and walk along the footpath. There is a field to my right with a wooden fence and trees on my left 4.I pass a house with hanging baskets with flowers in and a large garden 5.The front door is green
Section 2	1.There is a cul-de-sac on the right named Ashfield close 2.The tarmac path slopes down the hill 3. At the bottom of the hill is a school. 4. In the playground there is a hop-scotch grid marked out 5. The playing field has football posts and changing hut.
Section 3	1. I carry on pass the school and at the end of the road I can see the pub in front of me. 2. The building is painted yellow and has a sign saying 'The Crown' 3.There is a beer garden with a wooden fence around it 4.Ther are six tables with sun umbrellas 5.In turn left at the pub into Heath Road
Section 4	1.I pass houses on my right with high garden walls 2.Over the top of the walls I can see ivy growing over the top and tall trees behind 3.As I walk into the main village I can see the village green 4. There is an old red telephone box which now used as a village 'book swap ' There is a sign saying 'Help yourself' 5.The footpath begins to go up the hill
Section 5	1.The path leads into open fields. 2. There are hedgerows dividing the fields 3. I turn right to climb over a style to follow the path 4. The path is now narrow - just earth and grass 5. In the distance I on the right can see farm buildings
Section 6	1.I walk towards the small wood in front of me 2.Through the trees I can see the road in front of me 3. I go through the metal gate and close it behind me 4. I follow the road back towards the village past the 30 mph traffic sign 5. The allotments are now on my right .
Section 7	1.There is a small brown wooden shed with a grey felt roof. The door faces the road and is secured by a large metal lock 2.There are neat rows of separate allotments with red plot markers for each section 3.I pass the green metal fence and double gates. 4.I am now back in the village with houses both on my left and right 5.The news agents is on my left.
Section 8	1 The newsagents has a red post office sign above the door 2. Through the window I can see shelves stacked with groceries 3.The post office counter is at the back of the shop with a glass screen and weighing scales for parcels 4.There is a window box but no flowers 5.There is a disabled parking area for one car
Section 9	1.I turn left at the pedestrian crossing 2. I pass the road sign at the corner of the road which reads Turlington Road. The paint is peeling and faded 3. I pass the Co-op supermarket 4.There is a car park to the left 5 I can see the area for shopping trollies
Section 10	1. I pass a row of 3 bungalows on the right 2.Next to the bungalows is the village hall with its 'All welcome sign' 3. The church is next to the village hall. It has a square tower with a metal clock face. 4.There are grave stones some very old and leaning over 5.The trees have joined together over the path forming an arch

Methods: HTW-fMRI Paradigm Presentation

- Preparation

Home Town Walking Task

- You will see “Walk” on the screen
- Visualise a section of your walk in your head, focussing on what you can see, hear and smell around you

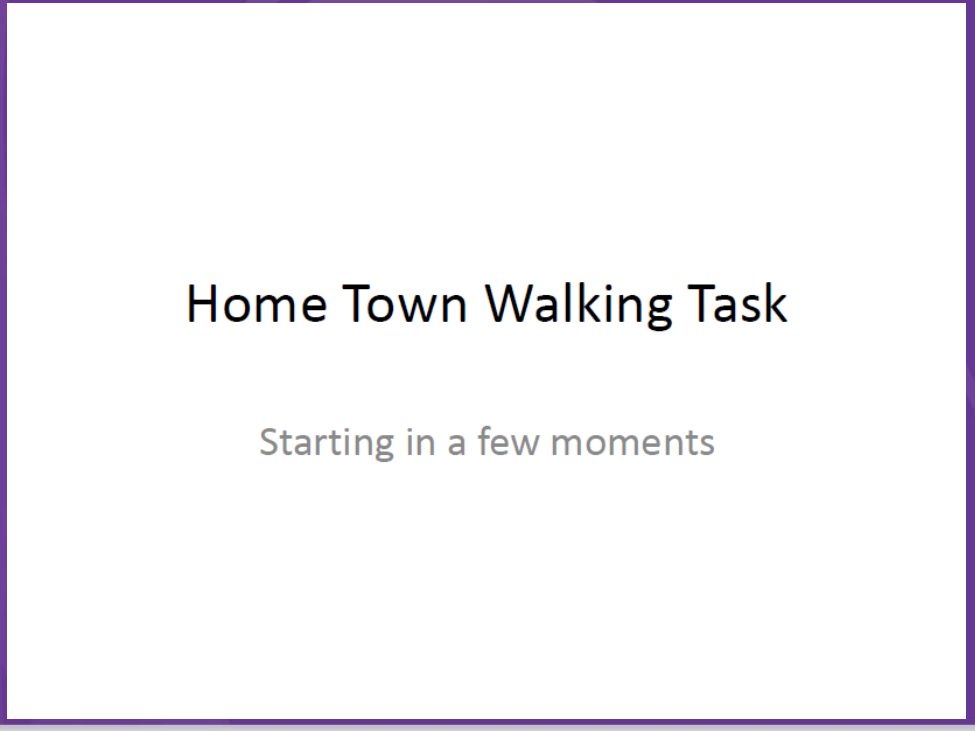
- **Imagine doing the walk in real life!**
- **The stronger you can picture your walk in your head, the better the scan will be!**

- In between walk sections, the screen will ask you to count backwards from 100 – do this in your head until the next walk section

- Alternating 30 second blocks of walking and counting
- Lasts 10 minutes in total

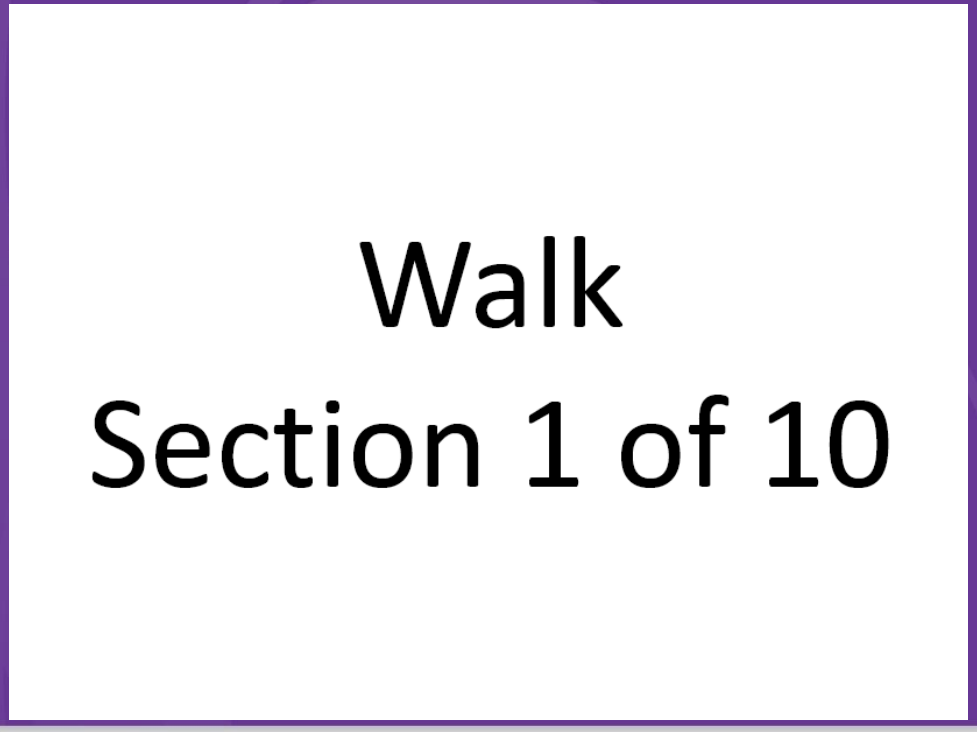
Methods: HTW-fMRI Paradigm Presentation

- Preparation



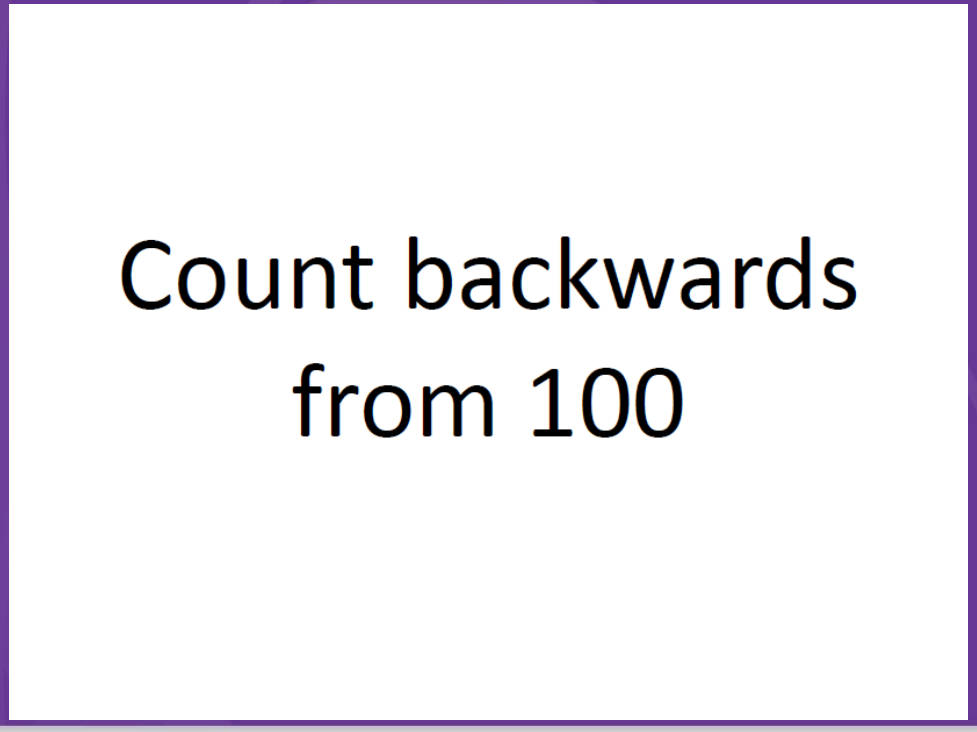
Methods: HTW-fMRI Paradigm Presentation

- Task block 1 (30s)



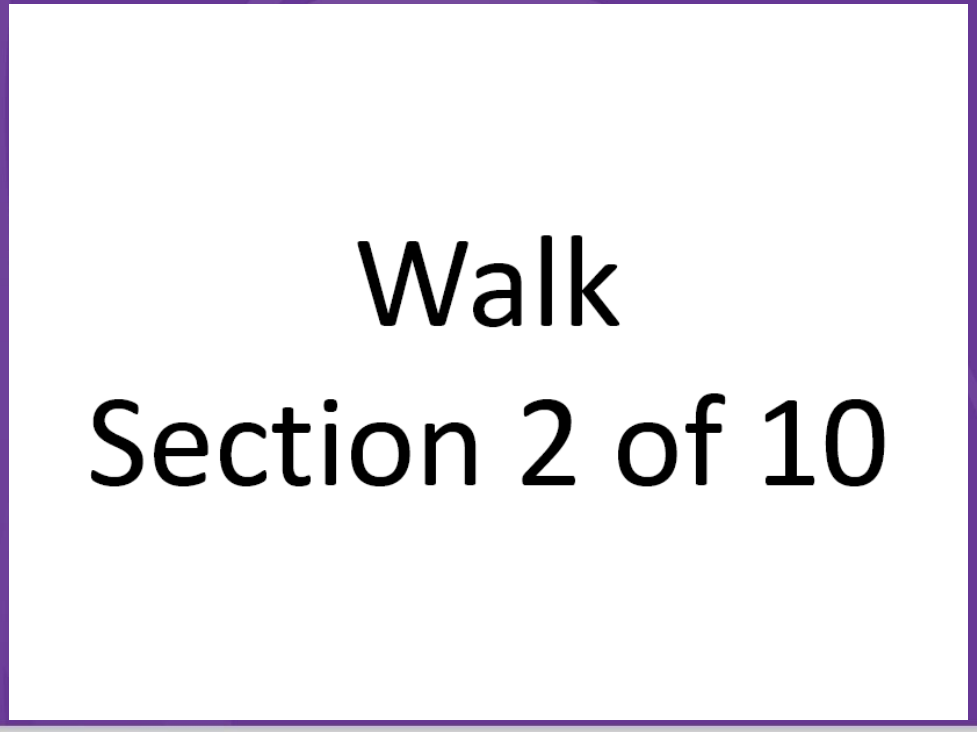
Methods: HTW-fMRI Paradigm Presentation

- Rest block 1 (30s)



Methods: HTW-fMRI Paradigm Presentation

- Task block 2 (30s)



Methods: Analysis - clinical

- fMRI data were first analysed using the manufacturer's software by an experienced consultant neuroradiologist
  - ❑ Workstation based "Neuro3D" application / Server based "Syngo.via"
  - ❑ Subjectively varied t-statistical map threshold & minimum cluster size
  - ❑ Optimised perceived balance between PHG activation and spurious
  - ❑ Produced clinical reports for surgical planning including comments on
    - Presence and reliability of PHG / memory-specific activation
    - Whether it was bilateral or predominantly left or right sided

Methods: Analysis - validation

- PHG activations from repeated fMRI sessions were verified by MR physicists and compared with clinical reports
- Patient episodes were enumerated and patients classified according to the reproducibility of the PHG activation pattern:
  - ❑ Group A: Day 1 PHG activation pattern reproduced on Day 2
  - ❑ Group B: Different PHG activation pattern on Day 1 or Day 2
  - ❑ Group C: No reliable PHG activation on Day 1 or Day 2
- A balanced subset of 32 episodes were selected and analysed with FSL software to validate the results achieved with clinically approved tools

Methods: FSL (FEAT) Analysis

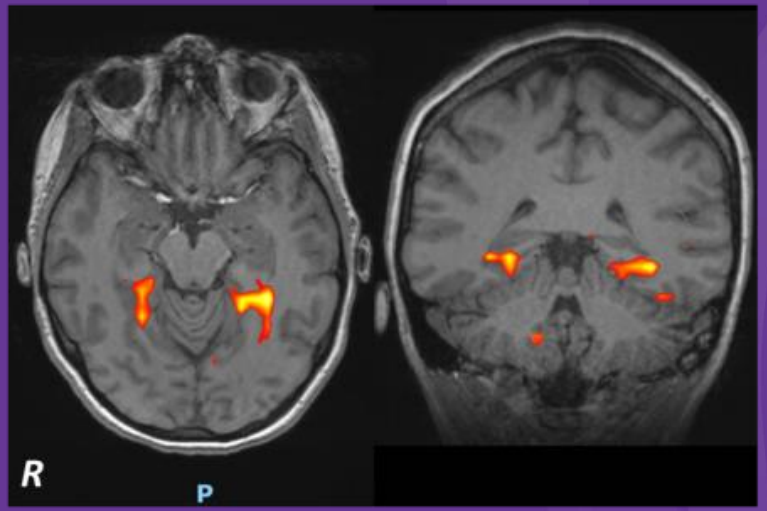
- Standard pre-processing (spatial smoothing; 5mm kernel)
- GLM fit using a gamma function model of HRF including temporal derivative
- Statistical maps: $z > 3.1$ and cluster corrected ($p<0.5$)
- Activation maps projected to a reference T1-w anatomical volume (day 1)
- Probabilistic masks of posterior PHG (right and left) created from Harvard-Oxford atlas, projected to each patient's reference space (using "fnirt")
- Statistical maps interrogated to display intersection & union of PHG activations
- Dice Coefficients (DC) computed: intersection / union volume ratio across days
  - ❑ DC > 0.15 considered "reproducible"

Results: Sample

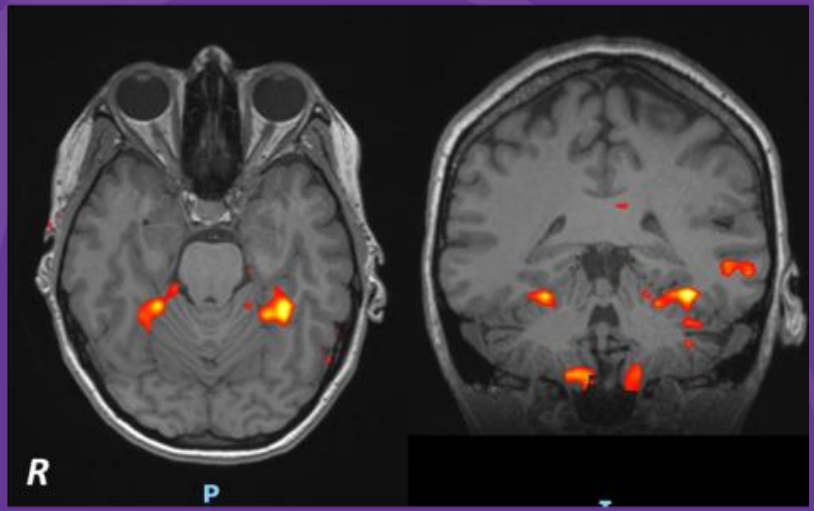
Total HTW-fMRI patient events	246
Total unique patient IDs	117
Patients with only 1 HTW-fMRI event	9
Patients with at least 1 repeat-HTW-fMRI episode	107
Patients with 2 repeat-HTW-fMRI episodes	9
Patients with 3 HTW-fMRI events per episode	5
Total episodes with repeated HTW-fMRI	**116**

Results: Clinical analysis using Syngo.via

Day 1



Day 2



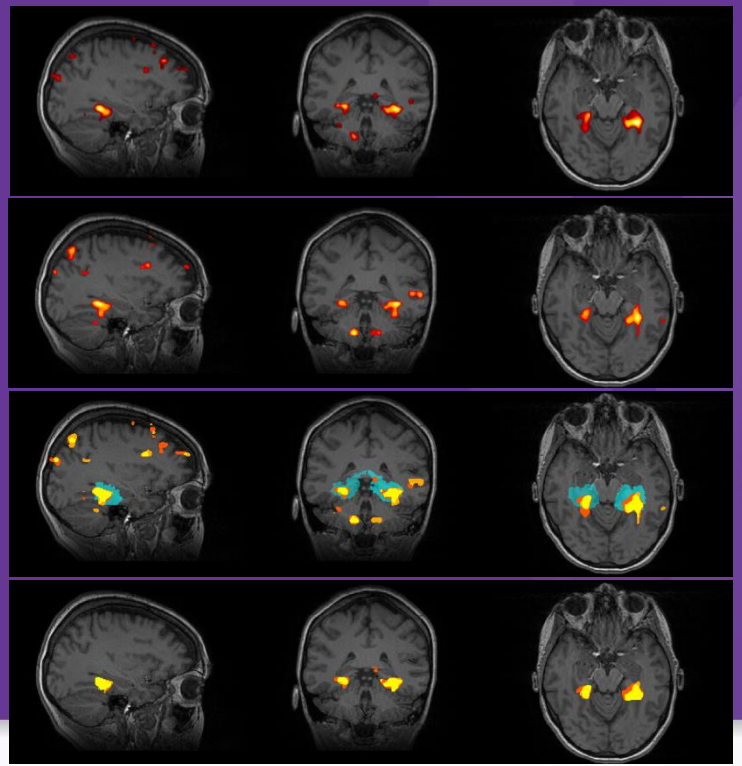
- Notes from report:

"Showed strong bilateral symmetrical activation in parahippocampal gyri"

Results: Clinical Analysis

	Day 1	Either Day	Group A (Reproduced)	Group B XOR(D1 ,D2)	Group C (No Activation)
PHG activation	69 (59%)	85 (73%)	63 (54%)	22 (19%)	31 (27%)
“Bilateral”			41 (65%)		
“Left dominant”			18 (29%)		
“Right dominant”			4 (6%)		

Results: FSL Analysis



Z-stat map from day 1 projected onto T1-w anatomical reference volume

Z-stat map from day 2 projected onto T1-w anatomical reference volume

Activations from both days combined:

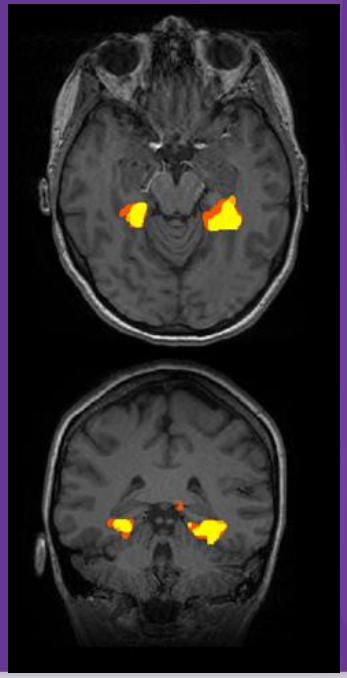
Day 1 *Day 2* *Intersection*

Probabilistic PHG regions

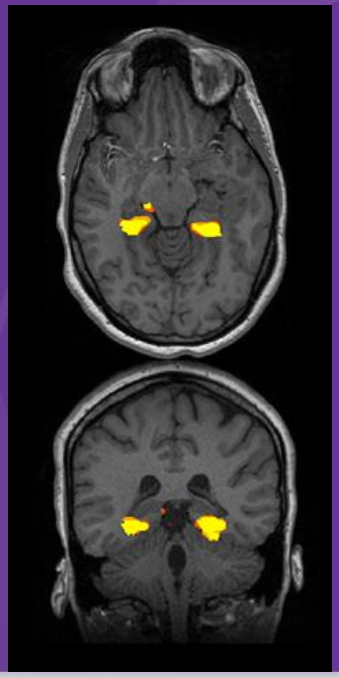
PHG Dice Coefficient across maps from both days:
DC = 0.59 (left PHG), DC = 0.41 (right PHG)

Results: FSL Results Examples

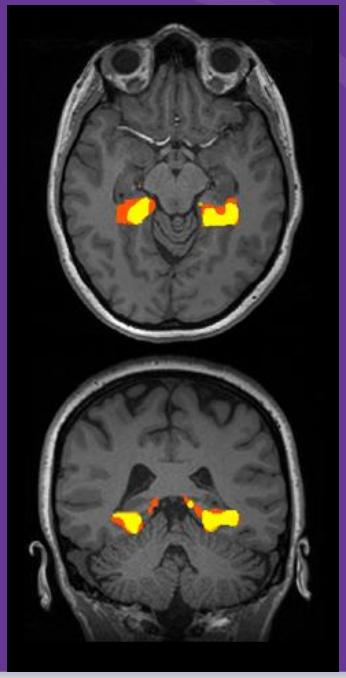
- *Day 1*
- *Day 2*
- *Intersection*



Group A

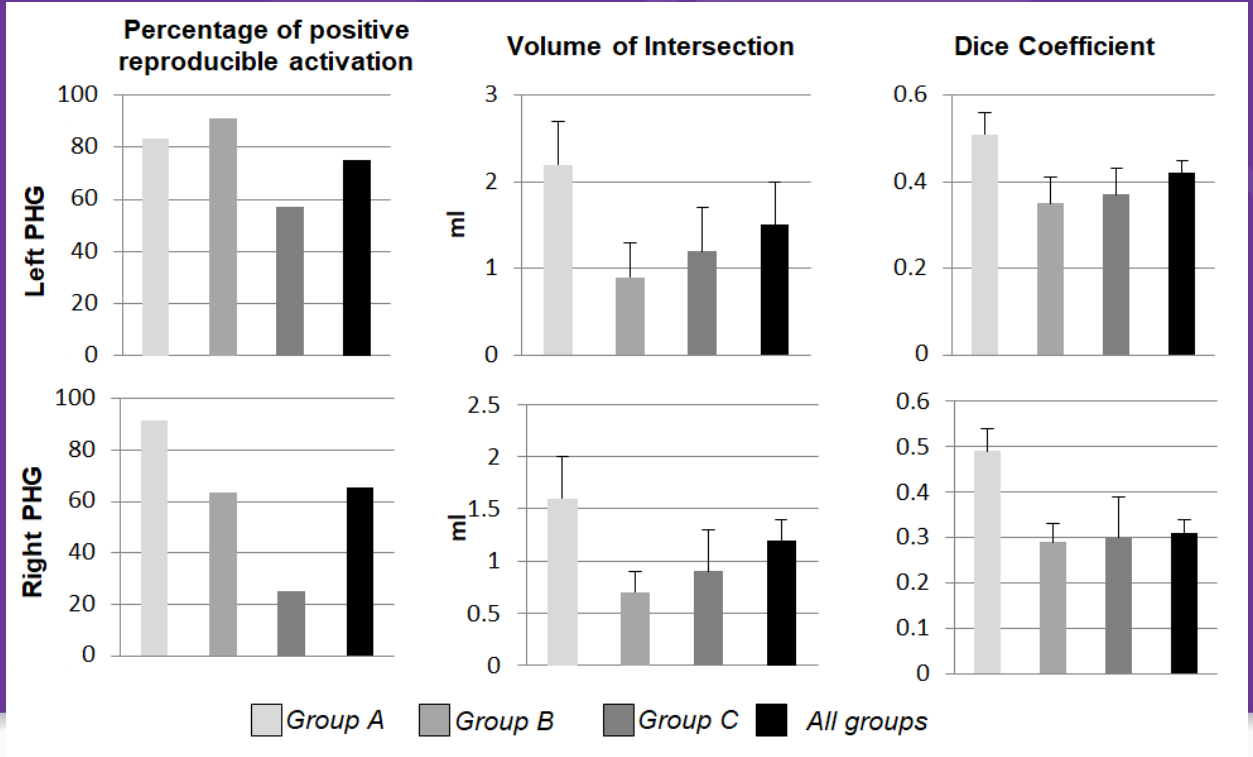


Group B



Group C

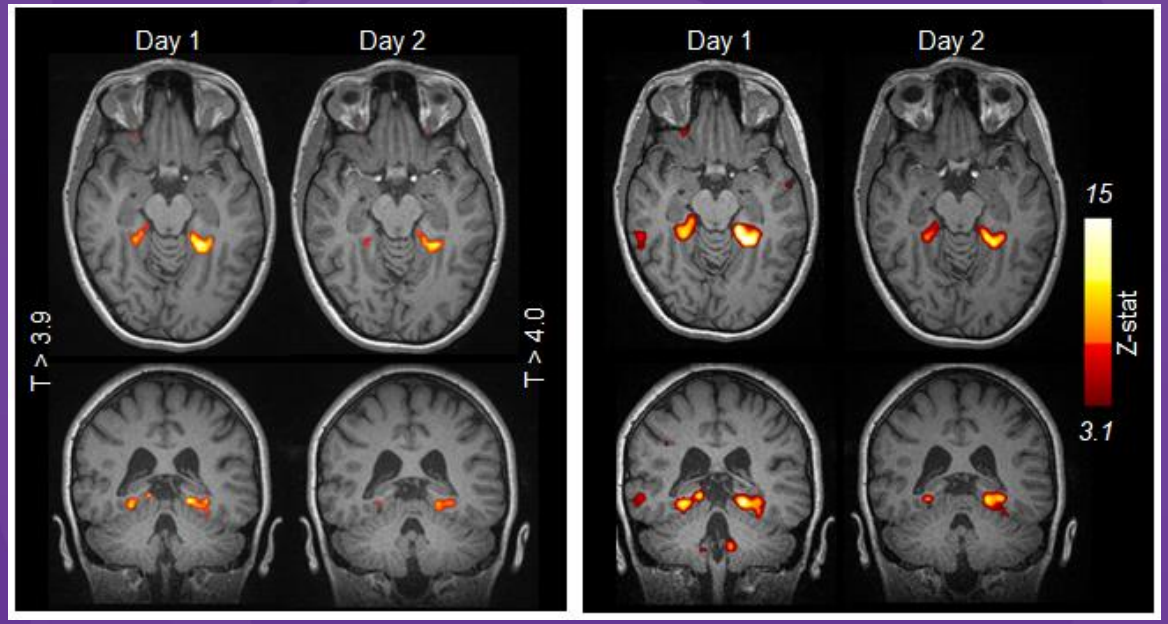
Results: FSL Group Analysis



Results: Siemens Neuro3D vs FSL

Example episode from Group A:

- “Reproduced PHG activation” on clinical report
- FSL analysis shows good agreement

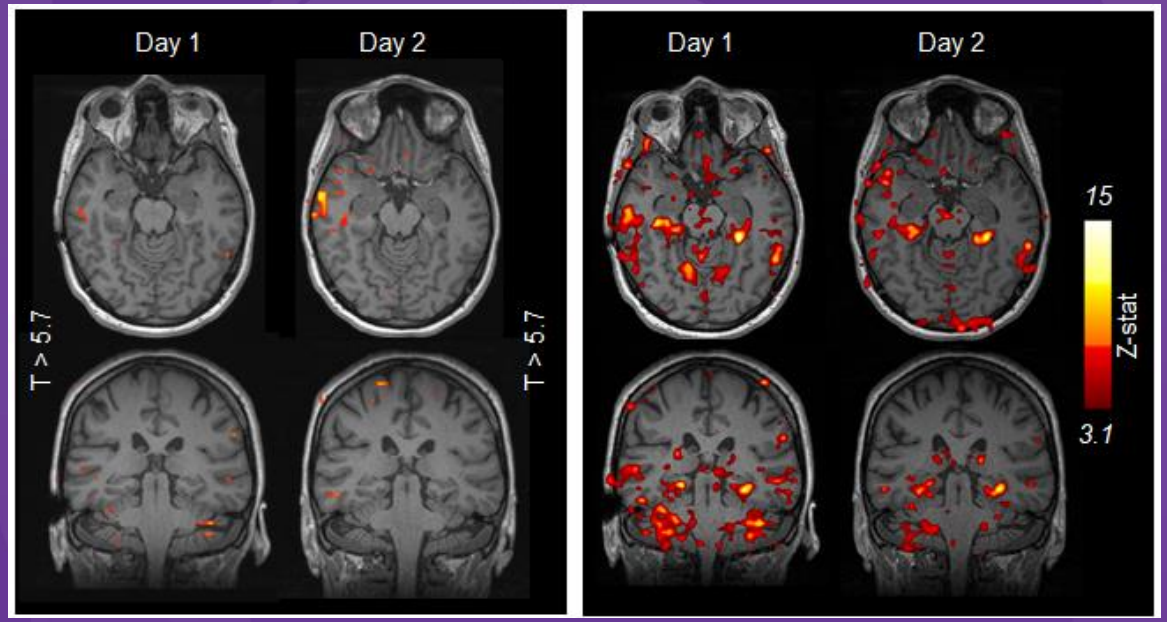


Siemens Neuro3D **FSL**

Results: Siemens Neuro3D vs FSL

Example episode from Group C:

- “No PHG activation found on day 1 or day 2” on clinical report
- Reproducible PHG activation on FSL



Siemens Neuro3D **FSL**

Results: FSL Results Summary

Groups from Clinical Analysis	Group A (Reproduced)	Group B XOR(D1, D2)	Group C (No Activation)
FSL Analysis Subset	13	12	7
Episodes with reproduced PHG activation	12	7	4
%Episodes with reproduced PHG activation	92%	58%	57%
Reproduced PHG activations projected for whole dataset using FSL analysis	58	13	18
	77%		

Discussion

- Despite being relatively difficult, most patients were able to perform the task given adequate preparation
- Reliable PHG activations were observed in the majority of cases using subjective clinical analysis, sometimes requiring more than 2 visits
- FSL analysis validates the subjective clinical results and potentially offers increased sensitivity and reliability if implemented clinically
- Future work will assess the correlation of fMRI results with postoperative memory outcome

Conclusions

- Implementation of the HTW fMRI paradigm is feasible in clinical practice
- Repeated HTW scans show reproducible BOLD activations in the medial temporal lobes sufficient to lateralise memory function
- HTW fMRI is a useful adjunct to neuropsychological memory assessment in epilepsy patients undergoing pre-surgical evaluation

Acknowledgements

- All of the RRPPS MRI Physics Team; especially Rosa Sanchez-Panchuelo who has led on the FSL analysis

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