

Preventing visual field deficits from neurosurgery

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ABSTRACT

Objective: We assessed whether display of optic radiation tractography during anterior temporal lobe resection (ATLR) for refractory temporal lobe epilepsy (TLE) can reduce the severity of post-operative visual field deficits (VFD) and increase the proportion of patients who can drive and whether correction for brain shift using intraoperative MRI (iMRI) is beneficial.

Methods: A cohort of 21 patients underwent ATLR in an iMRI suite. Preoperative tractography of the optic radiation was displayed on the navigation and operating microscope displays either without (9 patients) or with (12 patients) correction for brain shift. VFD were quantified using Goldmann perimetry and eligibility to drive was assessed by binocular Esterman perimetry 3 months after surgery. Secondary outcomes included seizure freedom and extent of hippocampal resection. The comparator was a cohort of 44 patients who underwent ATLR without iMRI.

Results: The VFD in the contralateral superior quadrant were significantly less ($p = 0.043$) with iMRI guidance (0%–49.2%, median 14.5%) than without (0%–90.9%, median 24.0%). No patient in the iMRI cohort developed a VFD that precluded driving whereas 13% of the non-iMRI cohort failed to meet UK driving criteria. Outcome did not differ between iMRI guidance with and without brain shift correction. Seizure outcome and degree of hippocampal resection were unchanged.

Conclusions: Display of the optic radiation with image guidance reduces the severity of VFD and did not affect seizure outcome or hippocampal resection. Correction for brain shift is possible but did not further improve outcome. Future work to incorporate tractography into conventional neuro-navigation systems will make the work more widely applicable. *Neurology*® 2014;83:604–611

GLOSSARY

ATLR = anterior temporal lobe resection; **DTI** = diffusion tensor imaging; **ILAE** = International League Against Epilepsy; **iMRI** = intraoperative MRI; **IQR** = interquartile range; **LGN** = lateral geniculate nucleus; **NHNN** = National Hospital for Neurology and Neurosurgery; **TLE** = temporal lobe epilepsy; **UQ** = upper quadrant; **VFD** = visual field deficit.

Anterior temporal lobe resection (ATLR) is an effective treatment for refractory temporal lobe epilepsy (TLE).¹ Surgical damage to Meyer loop, the most anterior part of the optic radiation, results in a visual field deficit (VFD) in between 48%² and 100% of patients.³ This precludes driving, a key goal of surgery,⁴ in 4%–50% of patients even if seizure-free.^{5–7}

Optic radiation fibers passing from the lateral geniculate nucleus (LGN) anteriorly over the roof of the lateral ventricle before turning backwards (Meyer loop) represent the superior visual quadrant so surgery may cause a contralateral superior quadrantanopia. VFD are hard to predict as the anterior extent of Meyer loop is variable⁸ and cannot be visualized intraoperatively. Diffusion tensor imaging tractography enables in vivo delineation of the optic radiation that can be used for epilepsy surgery planning.^{9,10} Preoperative imaging has been used in

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neuronavigation systems to guide surgery¹¹ but brain shift following craniotomy renders preoperative imaging inaccurate.¹²

Intraoperative MRI (iMRI) allows updated images to be acquired during surgery. Tractography can be repeated using deterministic algorithms,¹³ but these depict Meyer loop poorly.¹⁴ More accurate probabilistic algorithms can be performed on preoperative data but are too time-consuming to employ during surgery. While preoperative tractography can be superimposed on intraoperative imaging, current commercial systems use rigid registration that does not compensate for brain shift.

We developed computational techniques that update preoperative tractography to compensate for brain shift, showed that this technique could accurately predict the degree of VFD using postoperative imaging,¹⁵ and subsequently extended it for intraoperative imaging.¹⁶ We suggested that “real-time display in a neuronavigation suite of the location of the optic radiation will be highly beneficial in avoiding surgical damage”.¹⁵

In the current study, we first assess whether display of tractography during ATR can reduce the severity of VFD and increase the proportion of patients who can drive without affecting seizure outcome. Second, we assess whether correction for brain shift during surgery using iMRI confers additional benefit.

METHODS Subjects. We studied 21 consecutive patients (age range 23–63 years; median 36 years; 8 male) with medically refractory TLE undergoing ATR with intraoperative MRI at the National Hospital for Neurology and Neurosurgery (NHNN), Queen Square, London, UK, in 2012. All patients had structural MRI scans performed at 3T, video EEG telemetry, neuropsychology, neuropsychiatry, and if necessary intracranial EEG recordings prior to surgery. Structural MRI scans, diffusion tensor imaging (DTI), and visual fields were acquired before surgery and 3 months following surgery (range 70–145 days). Patient demographics and clinical data are listed in the table.

Bias was minimized by using consecutive patients operated with iMRI from a single center. As the first study employing intraoperative MRI, the study was an open cohort with comparison against historical controls so study size was limited by patient flow and duration of recruitment.

Standard protocol approvals, registrations, and patient consents. The study was approved by the NHNN and the Institute of Neurology Joint Research Ethics Committee. Informed written consent was obtained from all subjects.

Comparison cohort. For comparison to previous clinical practice, a cohort of patients was selected who underwent the same assessment and basic technique for ATR by the same neurosurgeon in

a conventional operating theatre without tractography-based image guidance comprising 44 patients from 2009 to 2012 (age range, 17–68 years; median, 39 years; 17 male; 21 left, 23 right ATR). No patient had a preoperative VFD.

Optic radiation tractography. Preoperative and postoperative MRI studies were performed on a 3T GE Signa HDx scanner (General Electric, Waukesha, WI) as previously described.¹⁵ Tractography of the optic radiation was performed using the multitensor probabilistic index of connectivity model¹⁷ in the Camino toolkit.¹⁸

Intraoperative imaging and surgery. Patients underwent surgery in the iMRI suite at NHNN (figure e-1 on the *Neurology*[®] Web site at Neurology.org). The operating table is outside the 5 gauss line during surgery, allowing standard surgical instruments to be used. For intraoperative imaging, the patient was transferred to a 1.5T Siemens Espree scanner (Siemens Healthcare, Erlangen, Germany) with a dedicated operating room 8-channel magnetic resonance head coil (Noras, Hochberg, Germany) that incorporates a surgical headrest. Anatomical scans included a T1-weighted 3D FLASH sequence with $1.1 \times 1.1 \times 1.25$ mm resolution, diffusion-weighted images were acquired with single-shot echoplanar imaging, 2.5-mm isotropic voxels, and 64 directions with a b value of 1,000 seconds/mm², and a field map was acquired using a gradient echo acquisition. The workflow is shown in figure 1.

During surgery, the BrainLAB VectorVision sky navigation platform (BrainLAB, Feldkirchen, Germany) provides real-time tracking of surgical markers and tools and visualization. An OPMI Pentero confocal surgical microscope (Carl Zeiss Meditec, Jena, Germany) allows injection of colour overlays from the neuronavigation system. The location of the microscope's focal point is tracked using the navigation system and an array of 4 infrared reflectors mounted on the microscope's optical head. Outlines were projected onto the navigation and operating microscope displays with solid lines used to depict the shape of the object in the focal plane and dashed lines to show the maximum extent below it, thus allowing depth perception.

A variety of surgical approaches to the ventricle are possible, with some accepting a VFD.¹⁹ At our center, the surgeon performs a modified Spencer ATR,²⁰ approaching the ventricle from the floor of the middle cranial fossa via the collateral sulcus aiming to pass underneath the optic radiation. The first intraoperative scans (timepoint 1) were acquired after initial dissection. The outlines of the optic radiation and ventricle (manually delineated by a radiologist) were displayed to guide entry into the ventricle below the optic radiation (figures 2 and 3). The optic radiation was later displayed to allow the surgeon to disconnect the temporal stem by making a cut through the temporal stem to the amygdala while remaining anterior to the optic radiation. A second intraoperative scan (timepoint 2) was acquired at the end of surgery to confirm adequate resection of any lesion and mesial temporal structures, including the amygdala, which may be difficult to visualize, and to exclude any immediate complications such as hemorrhage.

Brain shift correction. In the first cohort of patients (9 subjects), preoperative imaging including tractography of the optic radiation was transferred to the neuronavigation system and registered to intraoperative images using BrainLAB. This performs only a rigid transformation, which does not correct for brain shift. Error margins of 1.5 mm in the anatomic antero-posterior direction and 1.5 mm isotropic were added to account for the lack of compensation for susceptibility artefacts and potential brain shift, respectively (figure 1).

Table Patient demographics, age at epilepsy onset, MRI findings, histologic diagnosis, ILAE outcome at 3 months and 12 months (where available), and postoperative VFD

Sex/age, y	Age at onset, y	MRI	Histology	ILAE 3 mo/12 mo	VFD, % of upper quadrant
Cohort 1 (9 patients)					
M/34	26	Left PHG DNET	DNET	1/1	17.9
F/30	29	Left temporal cavernoma	Cavernoma	1/1	22.8
F/31	18	Right HS	HS	1/1	41.0
F/44	19	Right temporal extra-axial mass	Epidermoid	1/3	11.0
F/36	23	Right amygdala lesion	Gliosis	2/2	0.0
F/32	25	Right temporal cavernoma	Cavernoma	1/1	2.4
M/40	8	Left HS	HS	1/1	19.1
F/44	30	MRI-negative (right)	EFS	1/2	41.7
F/46	18	MRI-negative (right)	Negative	4/4	5.5
Cohort 2 (12 patients)					
F/27	22	MRI-negative (right)	Gliosis	1/1	0.0
M/30	28	Right temporal cavernoma	Cavernoma	1/1	3.0
M/52	16	Left HS	HS	1/1	49.2
F/29	0.25	Left HS	HS	1/1	0.0
M/63	17	Left ITG dysplasia	Hamartoma	4/4	47.3
F/48	12	Right HS	HS	1/1	0.0
M/23	15	MRI-negative (right)	Gliosis	1/1	0.0
F/30	7	Previous right SAH for DNET	HS	1/2	14.5
M/47	12	MRI-negative (right)	EFS	1/3	23.6
F/42	21	Left HS	EFS	1/3	32.3
F/43	38	Left PHG cavernoma	Cavernoma	1/1	3.8
M/35	2	Previous right ATR, residual HS	HS	1/1	25.0

Abbreviations: ATR = anterior temporal lobe resection; DNET = dysembryoplastic neuroepithelial tumor; EFS = end-folium sclerosis; HS = hippocampal sclerosis; ILAE = International League Against Epilepsy; ITG = inferior temporal gyrus; PHG = parahippocampal gyrus; SAH = selective amygdalohippocampectomy; VFD = visual field deficit.

In the second cohort of patients (12 subjects), preoperative and intraoperative images were transferred to a separate workstation. The preoperative tractography had been previously corrected for image distortion due to gradient nonlinearities and magnetic susceptibility artefacts using custom written software that relies on field maps.²¹ If no field map was available, an error margin of 1.5 mm in the anatomic antero-posterior direction was added. The same corrections were applied to the intraoperative data followed by nonlinear registration of the combined preoperative T1-weighted image and fractional anisotropy map to the intraoperative imaging as previously described.¹⁶ The corrected images were transferred to BrainLAB for display. Processing was performed using graphical processing units to ensure the entire procedure could be performed quickly enough not to delay surgery.²² The image registration software is available for download under an open source license (<http://sourceforge.net/projects/niftyreg/>).

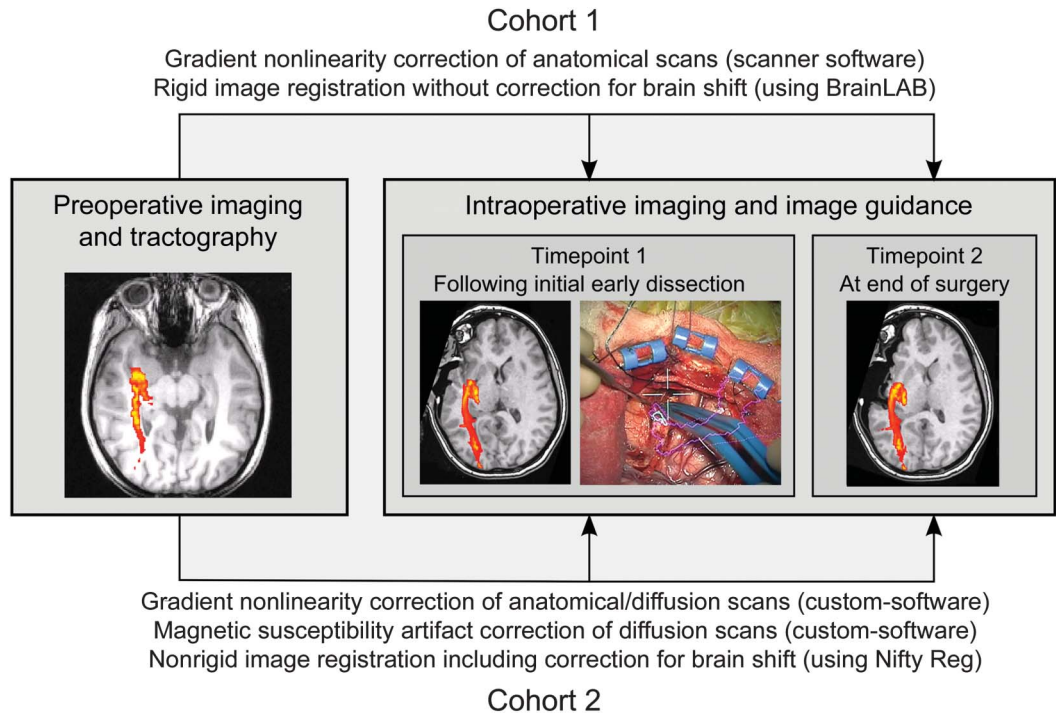
Primary outcome: Visual fields. Preoperative and postoperative visual fields were assessed using Goldmann perimetry. To quantify the VFD, postoperative visual fields were scanned and the areas enclosed by the V4e and I4e isopters in each upper quadrant (UQ) were determined. Visual field loss for each isopter was calculated as previously¹⁵ and the mean of the 2 figures was taken. The use of a single timepoint eliminates the high variability observed between Goldmann perimetry sessions.²³

$$\text{VFD} = 1 - \frac{(\text{area contralateral UQ [left eye]} + \text{area contralateral UQ [right eye]})}{(\text{area ipsilateral UQ [left eye]} + \text{area ipsilateral UQ [right eye]})}$$

The number of patients not permitted to drive due to the VFD was determined in accordance with UK Driver and Vehicle Licensing Agency regulations²⁴ with additional binocular Esterman perimetry if necessary. UK regulations are based on EU Directive 2009/113/EC that requires a horizontal visual field of at least 120° (at least 50° left and right) and 20° up and down with no deficits in the central 20°. These requirements were adopted following recommendations in a report of the Eyesight Working Group to the European Driving License Committee in 2005.²⁵ This review noted that while data were available confirming the importance of adequate visual fields for the safety of driving, there was a lack of data on the appropriate cutoff. The cutoff was therefore agreed by the expert panel, who suggested further research.

Secondary outcomes. To ascertain whether image guidance to avoid the optic radiation affected seizure freedom and the extent of hippocampal resection, seizure outcome at 3 months and 12 months was assessed using the International League Against Epilepsy (ILAE) classification²⁶ and the extent of resection was determined by measuring the antero-posterior extent of the residual hippocampus on postoperative imaging starting from the coronal

Figure 1 Pipeline for registration of preoperative and intraoperative images for display during surgery



The approaches for the 2 cohorts (without and with brain shift correction) are illustrated. Intraoperative images were acquired following initial dissection and at the end of surgery.

slice in which the greatest length of fornix was visible and moving anteriorly until no hippocampus remained.²⁷

After each operation, the surgeon completed a questionnaire concerning how the data affected the surgical plan, whether it was useful to improve the safety of surgery, and how it affected the duration of surgery. In view of the additional imaging time, the duration of scanning was recorded in 10 patients from cohort 2.

The degree of brain shift at the 2 intraoperative timepoints was assessed in cohort 2 using displacement fields generated from the nonlinear registration. The displacement in comparison to rigid registration was determined in the brain as a whole, in the optic radiation, and at the anterior tip of the temporal horn, a surgical landmark.

Statistical analysis. Statistical analyses were performed using PASW Statistics 18.0 (IBM, Armonk, NY). As VFD and degree of hippocampal resection were not normally distributed (Shapiro-Wilk test), the nonparametric independent-samples Mann-Whitney *U* or independent-samples Kruskal-Wallis tests were used to detect any difference in the distribution between groups. In contrast, the observed brain shifts were normally distributed (Shapiro-Wilk test).

RESULTS Visual field deficits. All patients were assessed following surgery. None of the 21 patients undergoing surgery with iMRI guidance developed a VFD that precluded driving. The VFD were 0%–41.7% of the contralateral superior quadrant (median 17.9%, interquartile range [IQR] 28.0%) in cohort 1, 0%–49.2% (median 9.2%, IQR 30.5%) in cohort 2, and 0%–49.2% (median 14.5%, IQR 27.5%) overall.

Four patients in the historical cohort had equivocal Goldmann perimetry but declined Esterman as they did not wish to drive. Of the remaining patients, 5/40 (12.5%) failed to meet driving criteria as a result of surgery. The VFD were 0%–90.9% of the contralateral superior quadrant (median 24.0%, IQR 32.6%).

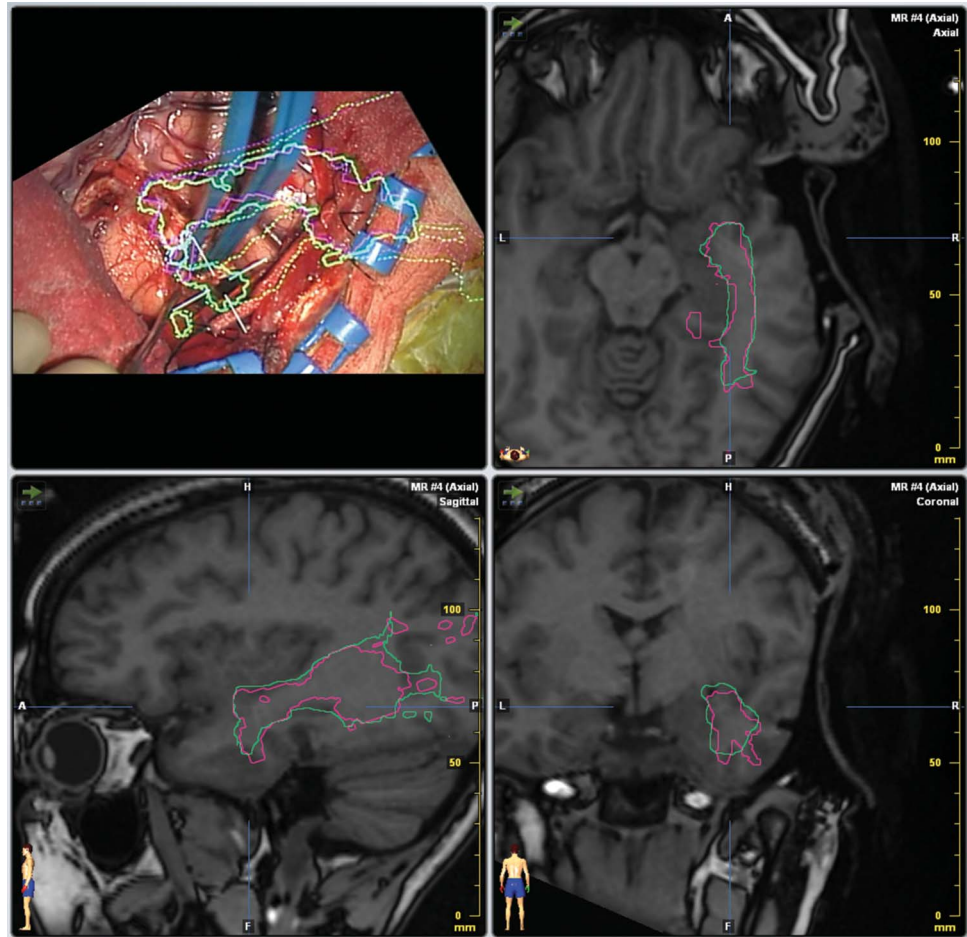
The observed VFD were due solely to damage to the optic radiation in all patients. There was no evidence of any additional pathology on postoperative imaging to explain the VFD such as cerebral infarction.

The distribution of VFD from those with iMRI guidance (cohorts 1 and 2 combined) was significantly different from those without iMRI guidance (figure e-2) (independent-samples Mann-Whitney *U* test $p = 0.043$). The difference was not significant between the historical controls and each iMRI-guided cohort individually.

In cohort 2, two patients had previous surgery, with one having a preexisting minor VFD that did not preclude driving. Exclusion of these patients did not affect the significant difference but the median VFD fell to 3.4% (IQR 36.0%) in cohort 2 and to 11.0% (IQR 32.3%) in the iMRI-guided cohort overall.

Seizure outcome. At 3 months, 89% of patients in cohort 1, 92% in cohort 2, and 91% in the historical cohort had a good outcome (ILAE groups 1 or 2) (table). At 12 months, 78% in cohort 1, 75% in cohort 2, and 84% in the historical cohort had a good outcome.

Figure 2 BrainLAB display of first intraoperative image following initial dissection during right anterior temporal lobe resection



The optic radiation before (pink) and after (green) correction for brain shift is superimposed with the solid outlines referring to the structure in the focal plane and the dashed outlines referring to the maximum extent below this. Note that BrainLAB shows right on the right (opposite to radiologic convention). In the top left panel, the operating microscope view with these outlines and the ventricle (blue) is shown flipped and rotated to correspond with the sagittal view (original microscope images are shown in figure 3).

Hippocampal resection. The median antero-posterior extent of remaining hippocampus was 15.4 mm (cohort 1), 16.0 mm (cohort 2), and 13.2 mm (historical cohort). There was no significant difference in the distribution between the groups (independent-samples Kruskal–Wallis test $p = 0.43$).

Surgeon's feedback. In all but 2 patients, the surgeon reported using a more anterior approach than in the historical cohort consequent to the display of the optic radiation, and imaging was particularly helpful in guiding safe entry into the anterior tip of the ventricle. In 4 patients, the degree of resection around the amygdala or temporal stem was altered in view of the anterior location of the optic radiation. The surgeon felt the data were helpful and made surgery safer in all subjects.

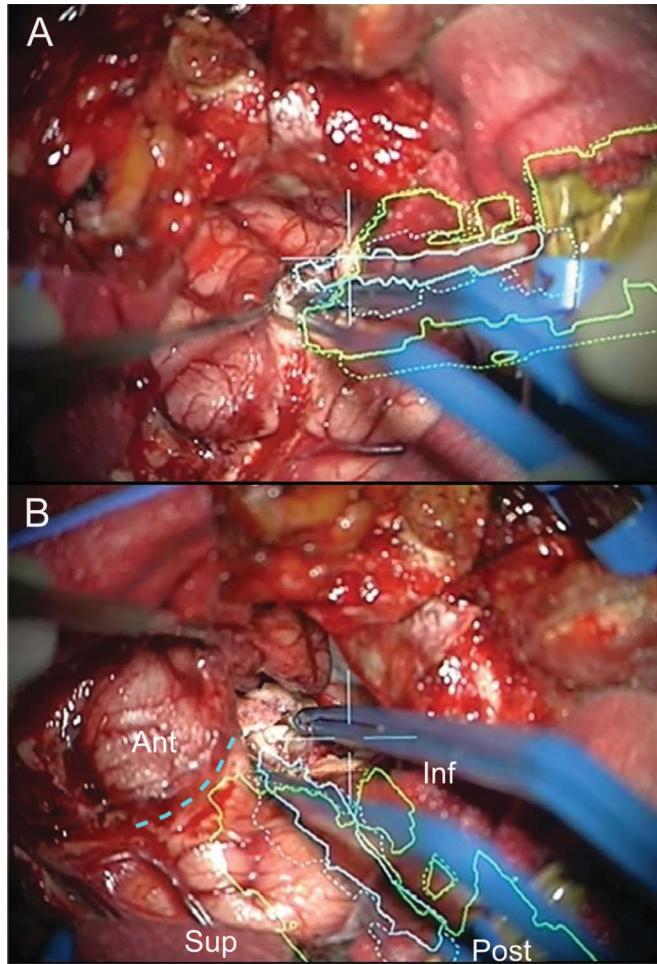
The duration of surgery was considered prolonged mainly by the scanning time. In one case, the surgery

was lengthened to try to avoid the optic radiation. It was commonly reported that resection was shortened by the ease in entering the ventricle.

Duration of scanning. The initial scan for neuronavigation took on average 31 minutes, measured from placing the magnetic resonance coil over the patient to removal of the coil (including transfer to/from the scanner and imaging time). The intraoperative anatomic/diffusion scans took on average 54 minutes and 47 minutes, respectively. In one patient, the second scan was not performed due to time constraints. A single patient developed a self-resolving brachial plexopathy following surgery.

Degree of brain shift. In the brain, the maximum displacements observed were 4.7–8.1 mm (mean 6.5 mm) at timepoint 1 and 8.7–13.8 mm (mean 10.9 mm) at timepoint 2. At the first timepoint, this was typically in the anterolateral temporal lobe or the

Figure 3 Operating microscope display of a patient undergoing right anterior temporal lobe resection



The head is rotated in the operating position as indicated in the lower panel. The superimposed outlines are the optic radiation (yellow-green) and the ventricle (blue). Solid outlines refer to the structure in the focal plane and dashed outlines refer to the maximum extent below this. (A) The surgeon approaching the tip of the temporal horn of the lateral ventricle from the middle cranial fossa while remaining inferior to the optic radiation. (B) The point of entry into the lateral ventricle exposing the hippocampus. The next step of the operation is to transect the temporal stem along the dotted blue line remaining anterior to the maximal projection of the optic radiation.

frontal lobe, and thus some distance from the optic radiation. In the operating position, these regions are the most superior, so subject to the greatest effects of gravity. At the second timepoint, the maximum displacements were seen superior or posterior to the posterior margin of the resection, where the brain sags into the void created.

Within the optic radiation, the maximum displacements were 2.8–6.8 mm (mean 4.3 mm) at timepoint 1 and 6.7–12.8 mm (mean 9.3 mm) at timepoint 2. These occurred in the anterolateral portion of Meyer loop or the part of the optic radiation just posterior to this. The displacement of the anterior tip of the lateral ventricle was only 0.9–3.2 mm (mean 1.9 mm) at timepoint 1, but this landmark was not visible at the second timepoint. In all cases, the landmark moved medially up

to 2.8 mm (mean 1.3 mm) while the displacement in the other orthogonal axes occurred in either direction. In particular, the antero-posterior displacement was negligible (1.3 mm anterior to 1.3 mm posterior, mean magnitude of displacement 0.5 mm).

DISCUSSION We have shown that display of the optic radiation with image guidance during ATLR reduces the severity of VFD and that no patient failed to meet visual criteria for driving as a result of surgery in comparison to 13% of recent historical controls. This was achieved with comparable seizure outcomes and hippocampal resection. We have shown that while it is technically possible to correct for intraoperative brain shift within neurosurgical time constraints, this did not further improve the outcome. The technique could be readily incorporated into surgery and the surgeon found it useful in all cases.

The inability to drive is one of the most important concerns of patients with epilepsy²⁸ and gaining a driving license is a key aim of patients undergoing surgery.⁴ Previous studies have shown that between 4% and 50% of patients fail to meet visual criteria for driving after ATLR.^{5–7} With improved imaging techniques, surgery may now be undertaken in previously ineligible patients, including neocortical or nonlesional epilepsy, where the risk to vision may be greater. Six patients (27%) in our image-guided cohort were nonlesional.

Serial imaging demonstrates progressive brain shift during tumor surgery.¹² Brain shift during ATLR has also been assessed by one group¹³ by performing deterministic tractography on a preoperative and single intraoperative image taken at the end of surgery. Around the resection area, shifts of up to 11.1 mm horizontally (mean 3.75 mm) and up to 7.8 mm vertically (mean 2.46 mm) were found, but were not used to guide surgery. In the present study, we demonstrated the maximum brain shift in the optic radiation was up to 6.8 mm (mean 4.3 mm) and up to 12.8 mm (mean 9.3 mm) at the 2 timepoints, confirming that brain shift develops during surgery.

Our previous study demonstrated that each additional 1 mm of damage to Meyer loop causes an additional loss of 5% of the upper quadrant.¹⁵ Meyer loop is closely related to the anterior tip of the lateral ventricle and is at risk during the early part of surgery. However, the displacement of this landmark was minimal (maximum 3.2 mm, mean 1.9 mm), with negligible movement in the antero-posterior direction, which is the most critical direction when attempting dissection anterior to the optic radiation. This small extent of brain shift explains the lack of additional benefit from correcting for intraoperative brain shift in ATLR over and above the addition of an error margin.

We employed probabilistic tractography and a robust algorithm to delineate Meyer loop of the optic

radiation. Visual and other outcomes were systematically assessed in all patients in both the iMRI-guided cohort and the historical cohort. While visual criteria for driving may differ between countries, guidelines in the United Kingdom and other European countries follow a European Union directive.

The intraoperative correction of all sources of image distortion, such as gradient nonlinearity and magnetic field inhomogeneities, and for brain shift took 8–9 minutes, the same time taken to transfer a patient from the scanner back to the operating table.

iMRI enables the assessment of completeness of resection and immediate surgical complications but the key limitations are the cost and imaging time prolonging surgery.

This study implies that display of optic radiation tractography in the operating microscope led to a change in surgical approach to avoid the optic radiation and mitigate the risk of causing a VFD.

As interventional MRI is expensive, prolongs surgery, and is not widely available, our next step is to assess the benefit of incorporation of probabilistic tractography of the optic radiation into the operating microscope display of a commonly used neuronavigation system such as StealthStation (Medtronic, Minneapolis, MN), which would make this advance widely applicable. In addition, we are exploring more economical ways of correcting for brain shift, such as intraoperative ultrasound.

AUTHOR CONTRIBUTIONS

Dr. Winston: drafting and revising manuscript, study concept/design, analysis/interpretation of data, acquisition of data, statistical analysis, study coordination, obtaining funding. Dr. Daga: revising manuscript, study concept/design, analysis/interpretation of data, contribution of software tools. Dr. White: revising manuscript, study concept/design, analysis/interpretation of data, acquisition of data. Dr. Micallef: study concept/design, analysis/interpretation of data, acquisition of data, obtaining ethical approval. Dr. Miserocchi: revising manuscript, acquisition of data, study coordination. Dr. Mancini: revising manuscript, study concept/design, analysis/interpretation of data, acquisition of data. Dr. Modat: study concept/design, contribution of software tools. J. Stretton: revising manuscript, acquisition of data. M.K. Sidhu: revising manuscript, acquisition of data. Dr. Symms: study concept/design, contribution of MRI acquisition sequences. Dr. Lythgoe: study concept/design, contribution of MRI acquisition sequences. Dr. Thornton: study concept/design, obtaining ethical approval. Dr. Yousry: revising manuscript, study concept/design, study supervision. Dr. Ourselin: study concept/design, contribution of software tools, study supervision, obtaining funding. Dr. Duncan: revising manuscript, study concept/design, study supervision, obtaining funding. Dr. McEvoy: revising manuscript, study concept/design, acquisition of data, study supervision.

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