

# Neurography Institute

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**Patient LAST Name:** XXXXX

**Patient FIRST Name:** XXXXX

**Accession #:** XXXXX

**Patient D.O.B.:** 01/01/1000

**Requesting Physician:** Smith, MD Fax: 111-111-1111

**DATE OF STUDY:** XXXXX

**Site Name and Equipment:** Resolution Imaging Santa Monica, CA 3T, Siemens MRI Scanner

**INDICATION:** This is a 31-year-old who on xxx2019 was involved in a motor vehicle collision in which they states that a vehicle ran a stop sign and impacted the vehicle on the passenger side, with the consequence of them impacting their head on a side window, wherein they report loss of consciousness and did suffer lacerations including a tongue laceration. Following the accident they experienced a variety of impairments affecting cognition, memory, mood, sleep-wake cycle, speech functions, and depression. A number of these symptoms have persisted.

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## **STUDY: MRI OF THE BRAIN WITH DIFFUSION TENSOR IMAGING**

**METHODS:** These images demonstrate the detailed anatomy of the brain with supplemental analysis through evaluation of fractional anisotropy and diffusion tensor imaging tractography.

The report is provided in three segments:

- 1) Tractography from diffusion tensor imaging (DTI)
- 2) Fractional Anisotropy analysis from diffusion tensor imaging (DTI)
- 3) General brain imaging with Susceptibility Weighted Imaging (SWI).

Diffusion tensor imaging (DTI) was obtained in a 3-Tesla Siemens imager using thirty directions of diffusion. The fractional anisotropy and tractographic analysis were processed using FDA approved NORDIC Brain Ex clinical workstation software.

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## **DTI TRACTOGRAPHY REPORT AND ANALYSIS:**

### **TRACTOGRAPHIC REPORT:**

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**TECHNICAL:** These images were obtained with 30 directions of diffusion gradients on a **Siemens 3-Tesla imager**, there are no significant artifacts impairing image interpretation.

The tractographic analysis is carried out by adjusting the fractional anisotropy threshold as well as the degrees of angulation and tractographic segment length as inputs to the FACT tractographic algorithm for tract analysis in order to identify areas of tractographic deficits and continuities.

Loss of tractographic continuity does not demonstrate a complete loss of connections; rather it is the effect of a decrease of coherently directed fractional anisotropy along the course of a tract. Such a dropoff halts the progress of the tractographic reconstruction process so that the remainder of the tract does not appear. These have clinical significance because they represent clinically relevant interference with transmission of neurological information from one part of the brain to another. The presence of such dropoff point does not represent complete loss or obstruction, but rather detects the presence of a relative drop off that affects the normal function of a major tract.

**FINDINGS:** Tractographic evaluation demonstrates significant losses bilaterally in the frontal lobes in the area of the white matter stem for the superior, middle and inferior frontal gyri. This type of abnormality can result in problems with multistep planning, map-based planning and emotional control release functions, correlating with some of her complaints about cognitive functional impairment. Losses are appreciated bilaterally in the supra-callosal cingulum which can result in increased depression and anxiety and this correlates with the patient's report of increased depression following the accident. Losses are seen in the mid-corpus callosum and this tractography abnormality is correlated with the presence of axonal shearing, diffuse axonal injury, which can have a general impact on cognition and is consistent with the impression from evaluating neurologist. There are symptoms of cognitive impairment reported to commence at the time of the accident. Losses are appreciated in the left arcuate fasciculus which in a right-handed individual would be expected to cause impairment of conversational speech. Additionally, a detailed formal tractographic analysis of the fornix and proximal limbic system was carried out and this demonstrated significant losses anteriorly in the pillar of the fornix on the right side and some more moderate losses in the crus of the fornix, also on the right side. This type of injury to the fornix will impair new memory formation and this correlates with the memory formation problems described by the patient as having onset in association with the accident. The parietal lobes are otherwise generally normal in appearance as to tractography. The temporal lobes are generally normal in appearance as to tractography. The occipital lobes are generally normal in appearance as to tractography. The cerebellar peduncles appear normal. Uncinate fasciculus and inferior fronto-occipital fasciculus bilaterally are normal in appearance. The right arcuate fasciculus is normal in appearance.

Three dimensional 360 degree rotations are provided in the DICOM data set for visualization of these findings.

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**TRACTOGRAPHY IMPRESSION:** Bilateral frontal lobe tractographic losses affecting the stem of white matter for the superior, middle and inferior frontal gyri with the expected effect of impairment of multistep planning, map-based planning and emotional control release functions, which correlates with some of the cognitive decline reported by the patient in association with the accident. Losses bilaterally in the supra-callosal cingulum which would have the effect of increased anxiety and depression, which correlate with history of increased depression described by the patient as a consequence of the accident. Losses in the mid-portion of the corpus callosum are consistent with the presence of a diffuse axonal injury that can have a general cognitive impairment effect, also correlating with the patient's description of general cognitive impairment in association with the accident. Losses are appreciated in the left arcuate fasciculus which would be expected to have effects on conversational speech in a right-handed individual and correlate with some of the speech dysfunction described by the patient as having onset at the time of the accident. A formal detailed tractographic analysis of the fornix and proximal limbic system demonstrates losses in the pillar of the fornix on the right side and the crus of the fornix on the right side as well with losses in the crus are more limited relative to the more significant loss in the area of the pillar anteriorly. This type of loss in the fornix would be expected to impair new memory formation and correlates with the history of impairment of new memory formation described by the patient as having onset in association with the accident. These abnormalities would be expected to have effects as described, affecting cognition, emotional behavior and neurologic functions as set forth in the findings above. The degree of abnormality appreciated in the imaging would be expected to result in clinically significant symptoms. The locations and types of injury are consistent with the mechanics of the trauma as described.

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#### **FRACTIONAL ANISOTROPY (FA) REPORT AND ANALYSIS:**

These images demonstrate the analytical level information concerning brain structure. The fractional anisotropy measurements are objective assessments of brain regions either obtained for standardization measurements or comparing right and left structures. Data is obtained with 30 directions of diffusion in a 3Tesla **Siemens scanner.**

**VOLUMES OF INTEREST (VOI's):** In all cases the volumes of interest (VOI's) that were measured are selected areas, entirely in white matter, of the highest intensity for fractional anisotropy as visualized by a fractional anisotropy overlay method. This method results in measurements of highest levels of fractional anisotropy in an anatomically recognizable brain white matter structure in the regions assessed. Data is provided with the size in cubic millimeters of the VOI, as well as the mean, minimum and maximum of FA values in the VOI with standard deviation calculated. Histograms are provided for each VOI that can reveal any unwanted bimodal distribution. Image captures were obtained demonstrating the location and size of each VOI measured as

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shown in three imaging planes. Further, the histograms provided show the variability of anisotropy among the voxels measured within each VOI. Significant right/left asymmetries in fractional anisotropy are considered clinically relevant on a prima facie basis. For a given level of anisotropy, a smaller size of a VOI – that is otherwise bilaterally symmetric – will reveal a reduced volume of that tract and this size difference also has clinical significance in many situations.

CLINICAL BASIS (Scientific Model): This fractional anisotropy analysis is carried out according to the method and clinical concept of Brander et al: *Diffusion Tensor Imaging of the Brain in a Healthy Adult Population: Normative Values and Measurement Reproducibility at 3 T and 1.5 T*; Acta Radiologica (2010), Volume 7 pages 800-807, in which VOI's are measured for fractional anisotropy using the Splenium of the Corpus Callosum as a baseline measure to be compared with other individuals as well as an internal references to assess relative FA dropoff in other brain regions. The data provided in articles such as the Brander study show expected relative fractional anisotropy measures using the Splenium of the Corpus Callosum as the standard, because this will tend to have the highest fractional anisotropy in the brain and can therefore provide a cross reference to other imaging subjects as well as provide a basis for assessing the degree of drop-off present to any given brain region associated in a relative to a comparative, standardized set of findings from large numbers of normal individuals.

There are more than 15,000 high quality peer reviewed publications showing the utility and clinical relevance of DTI and only one or two publications written by professional defense experts that attempt to formally raise concerns about utility (e.g. Wintermark, et al (2015), *Imaging Evidence and Recommendations for Traumatic Brain Injury: Advanced Neuro- and Neurovascular Imaging Techniques* AJNR 36:E1-E11) mostly by pointing out that the vast majority of publications use groups of patients (usually required for all published studies) but that legal cases focus on individuals. However, Wintermark provided an unreliable biased assessment because he improperly omitted excellent studies showing high clinical and legal utility of DTI data for individuals such as Yuh et al (2014): *Diffusion Tensor Imaging for Outcome Prediction in Mild Traumatic Brain Injury: A TRACK-TBI Study*, Journal of Neurotrauma 31:1457-1477; and Mustafi et al: *Acute White-Matter Abnormalities in Sports-Related Concussion: A Diffusion Tensor Imaging Study from the NCAA-DoD CARE Consortium*. Journal of Neurotrauma, ePub 2017.

CLINICAL BASIS (Report Methodology): By viewing an FA overlay on a high resolution, co-registered MP-RAGE three dimensional brain MRI acquisition, asymmetries and drop-offs can be identified as to identified anatomical brain structures. For these VOI locations, the mean and standard deviation data can be used to assess the statistical significance of any different in overall FA for a VOI compared with either the FA of the Splenium or with the FA of a similar VOI on the opposite side. Only a single combined FA for right and left Fornix is obtained in some cases because of its small size if it is not possible to obtain usable measures for each side.

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**SCIENTIFIC BASIS:** Fractional anisotropy is expressed as fraction between 0 and 1 and reflects the degree to which fibers within a given voxels or group of voxels measured and assessed in the volume of interest, tend to share a coherent single direction and high health with good quality within the measured volume. A loss of fractional anisotropy is correlated with a decrease of function or transmission to a given white matter tract area. When two different tracts pass through each other having different directions, incorrectly low FA levels can be obtained, but this is controlled for here by selecting well recognized white matter brain structures that have a coherent single direction. Additionally, matching the same structure right to left corrects for this directional diversity issue. As for comparisons with the Splenium FA values, the data from the Brander et al article provides a useful well documented clinical framework that corrects for the directional diversity issue.

**RESULTS (STANDARDIZATION):** The splenium of the corpus callosum has a fractional anisotropy of 0.87, which is well within normal range, and this is used as a baseline for comparison with other individuals and for comparison with other structures for this individual's brain as to fractional anisotropy.

**RESULTS OF FRACTIONAL ANISOTROPY ANALYSIS AND MEAN DIFFUSIVITY ANALYSIS (FINDINGS):** The splenium is commented on above. The genu of the corpus callosum is at 0.79, also within the normal range. The mid-portion of the corpus callosum is at 0.32, which is low. This would be consistent with evidence of diffuse axonal injury which can have a general impairment effect on cognition, correlating with some of the patient's description of cognitive impairment. The right corona radiata, measured at the level of the genu of the internal capsule is at 0.65, which is within the normal range, and for the left corona radiata measured at the level of the genu of the internal capsule is at 0.58, also within the normal range. On the right side of the frontal lobe measured at the stem of the white matter for the superior, middle and inferior frontal gyri, the fractional anisotropy is 0.45, just within the normal range and on the left side it is at 0.24, which is low. The right to left difference here is statistically significant and consistent with impairment of multistep planning, map-based planning and emotional control release functions, correlating with some of the cognitive impairment described by the patient with onset at the time of the accident. The right parietal lobe measures at 0.48, within the normal range. The left parietal lobe measures at 0.49, within the normal range. The right occipital lobe is at 0.54, within the normal range. The left occipital lobe is at 0.52, within the normal range. The right temporal lobe measures at 0.66, within the normal range. The left temporal lobe is at 0.63, within the normal range. The right uncinate fasciculus and inferior fronto-occipital fasciculus is at 0.59, which is within the normal range. The left uncinate fasciculus and inferior fronto-occipital fasciculus is at 0.60, which is within the normal range. The right arcuate fasciculus is at 0.39, which is low, and the left arcuate fasciculus is at 0.39 which is also low. For a right-handed individual, low numbers for the right arcuate fasciculus would be implicated for problems with prosody or flow of speech and the left arcuate fasciculus with more complex impairments of speech and conversational function, consistent with a

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history of problems with intermittent slurring of speech described by the patient with onset in association with the accident. The right hippocampal cingulum is at 0.33, which is low. The left hippocampal cingulum is at 0.37, which is also low. Low numbers for the hippocampal cingulum would be expected to result in impairment of attention, which can also affect memory formation processes. The right fimbria of the fornix and stria terminalis is at 0.56, within the normal range. The left fimbria of the fornix and stria terminalis is at 0.51, within the normal range. The anterior fornix in the area of the pillars is at 0.39, which is low. The posterior fornix at the level of the crus is at 0.45, which is within the normal range. The anterior to posterior difference is not statistically significant, although the anterior fornix number is moderately low, this can be implicated in problems with new memory formation. The basal forebrain area was evaluated for mean diffusivity, because it is a gray matter structure, by using a measurement of trace, which is three times the mean diffusivity. For the right side, the number is 328 and for the left side it is 335. These are moderately elevated. Elevation in the mean diffusivity is a sign of abnormality, which is inverse to the situation for fractional anisotropy where a lower number is significant for pathology. These elevated numbers for the basal forebrain suggest a problem with sleep function such as insomnia, which correlates with the patient's change in sleep process with increased insomnia following the accident. The right middle cerebellar peduncle is at 0.75, within the normal range. The left middle cerebellar peduncle is at 0.74, within the normal range. The right medial lemniscus is at 0.52, within the normal range. The left medial lemniscus is at 0.51, within the normal range.

**FRACTIONAL ANISOTROPY ANALYSIS AND MEAN DIFFUSIVITY IMPRESSION:** There is a low number for the mid-portion of the corpus callosum, indicative of some axonal shearing and diffuse axonal injury, which would be expected to result in some cognitive impairment, which correlates with the patient's description of some cognitive impairment. Low number for the left frontal lobe at the stem of white matter for the superior, middle and inferior frontal gyri with the expected effect of impairment of multistep planning, map-based planning and emotional control release functions. Low number for the arcuate fasciculus bilaterally with expected impairment on speech functions, correlating with the patient's description of slurring of speech following the accident. Low numbers for the hippocampal cingulum with expected impairment of attention, which can also affect memory formation consistent with the patient's history of recall problems during conversations. Low number for the anterior fornix, suggestive of problems with new memory formation. Elevation of mean diffusivity for the basal forebrain consistent with insomnia. Overall, these findings therefore have effects on cognition, emotional behavior and neurologic functions as set forth in the findings above. The degree of abnormality appreciated in the imaging would be expected to result in clinically significant symptoms. The locations and types of injury are consistent with the mechanics of the trauma as described.

**FA Measurements and Statistical Calculations:**

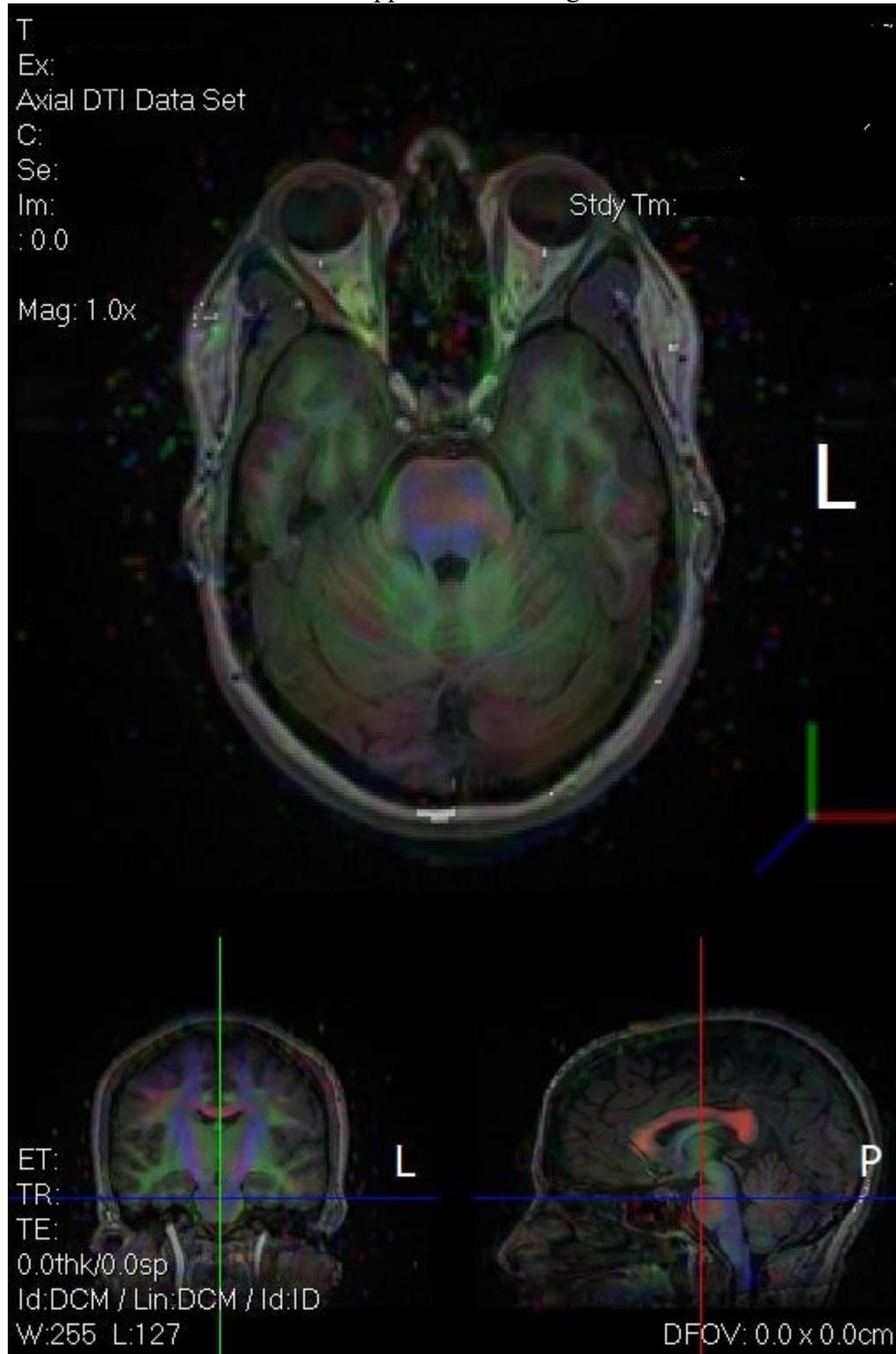
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This image demonstrates the measured VOI's for the medial lemniscus and the full data set. A full set of VOI measures appears in the image DICOM data file.

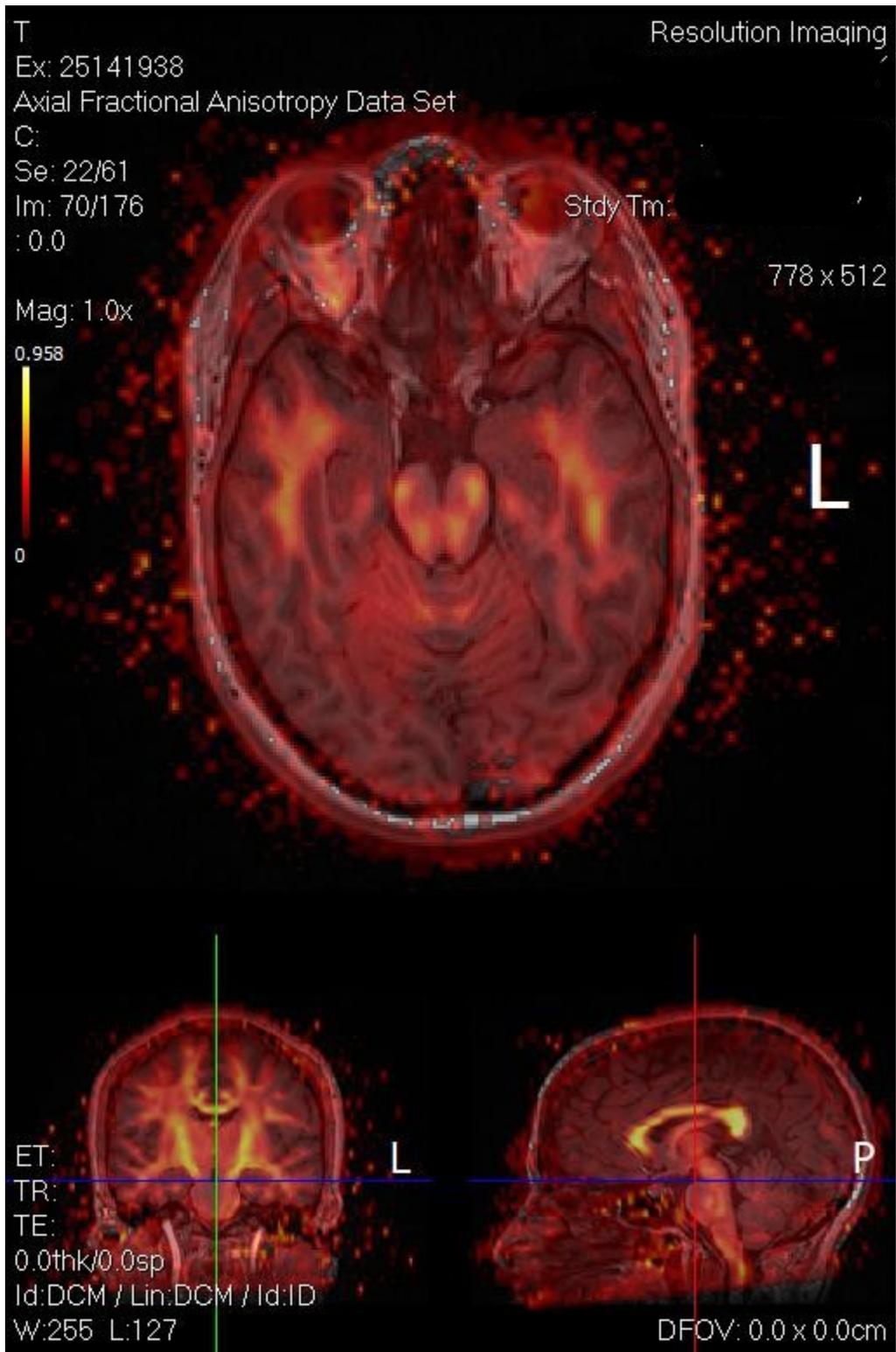


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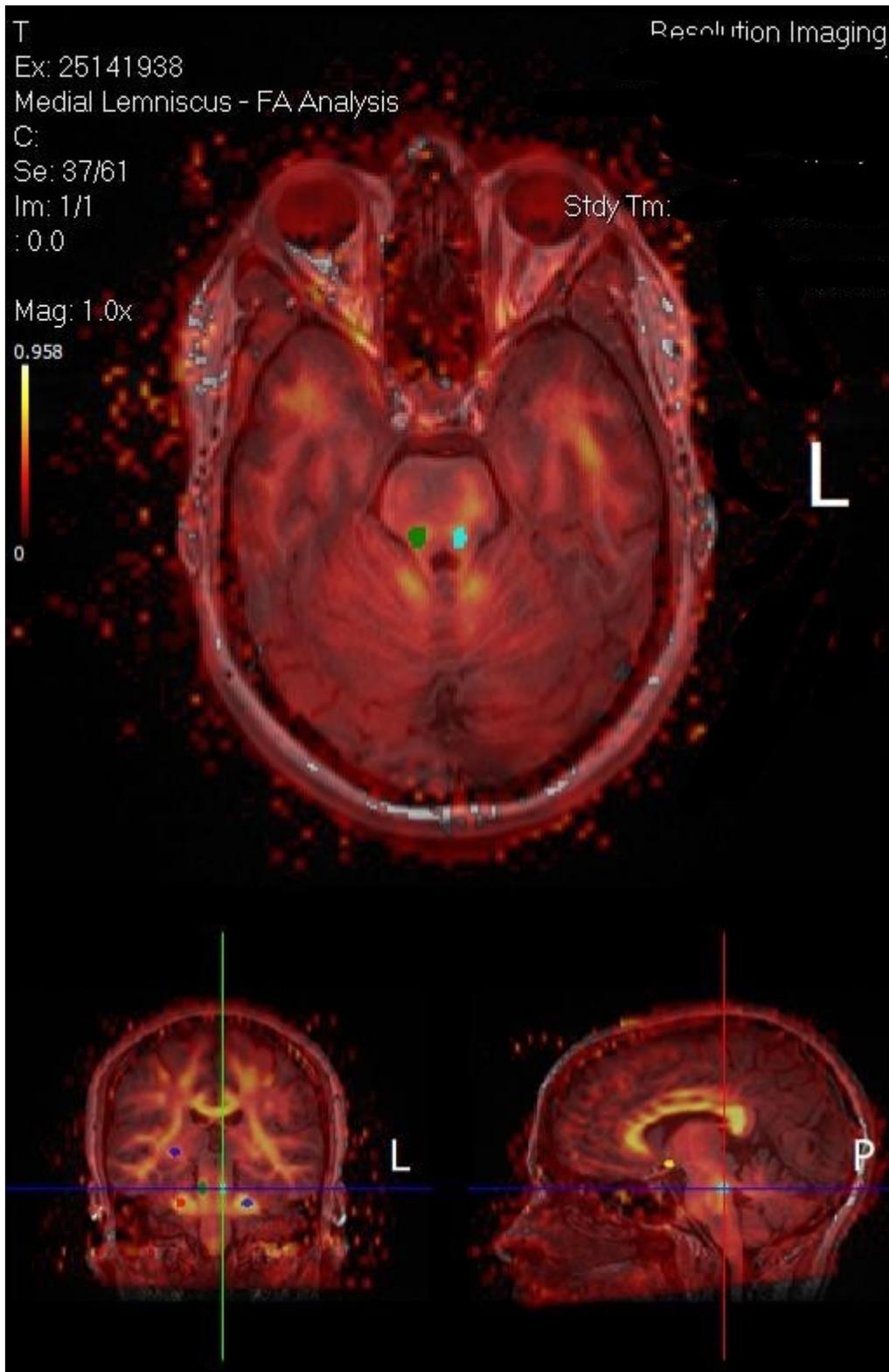


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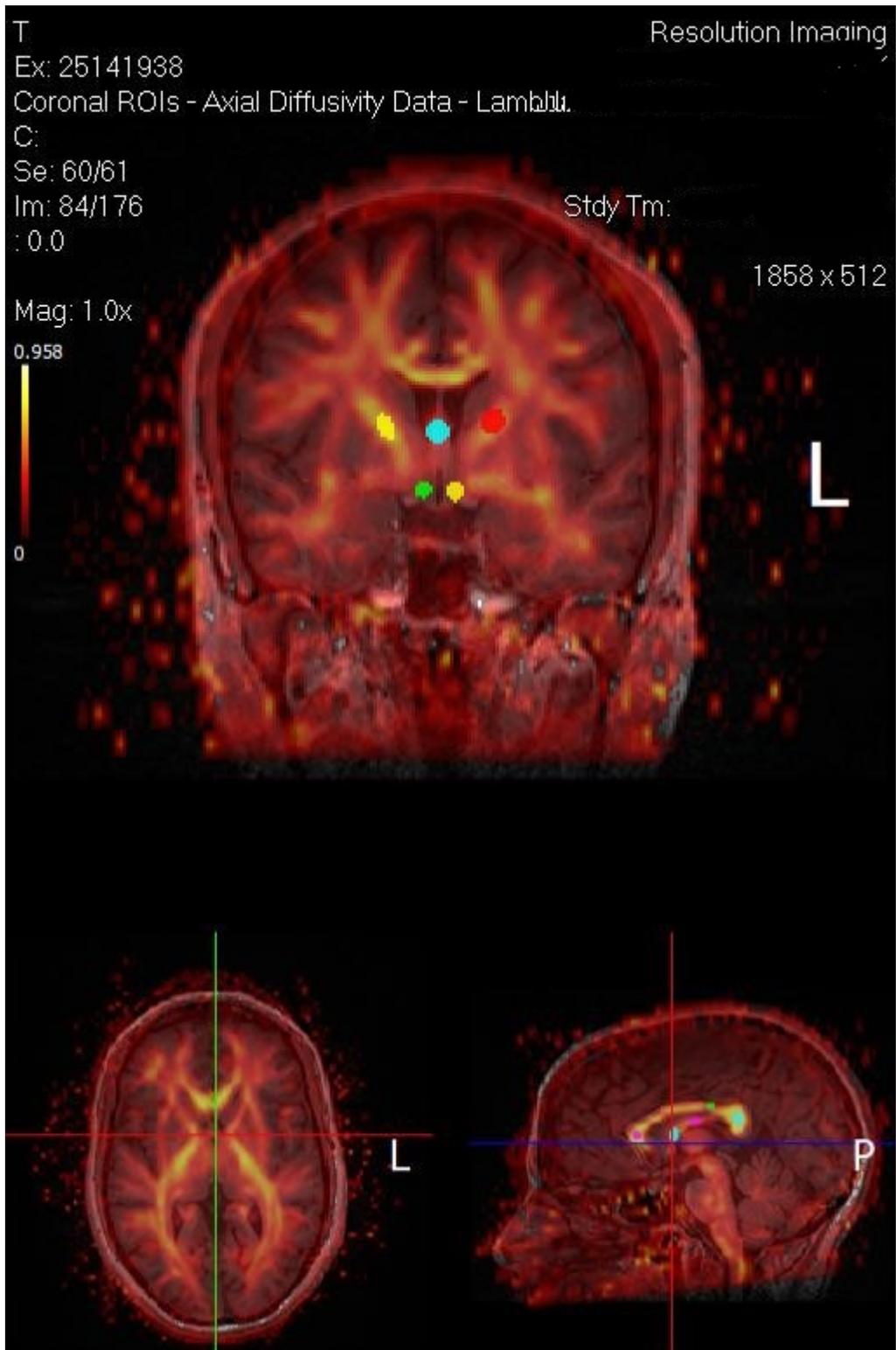


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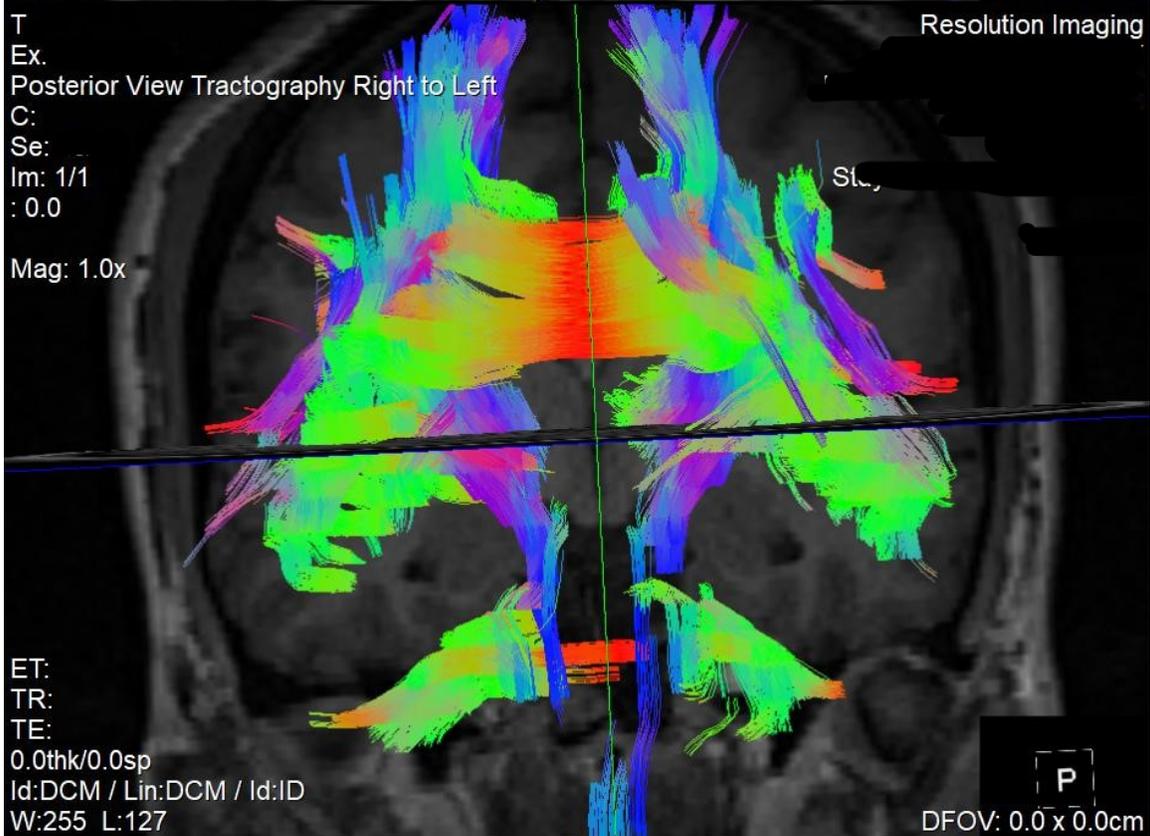
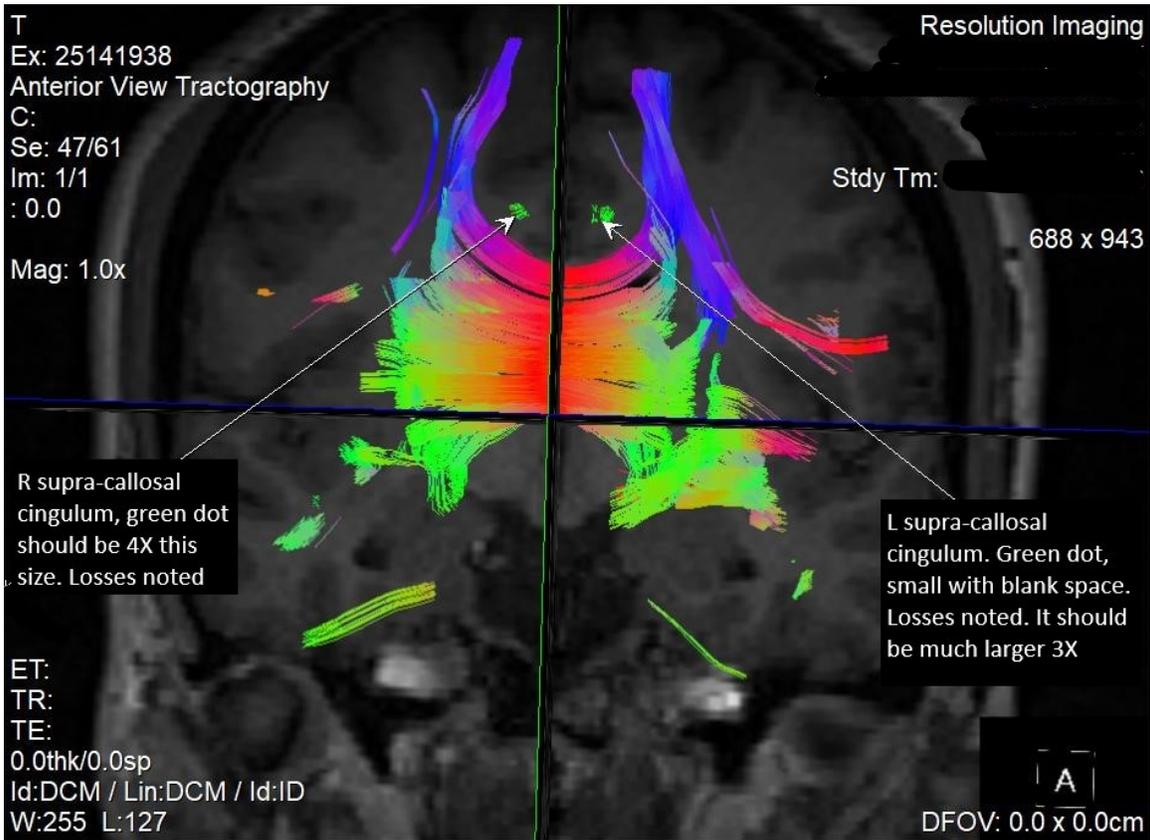


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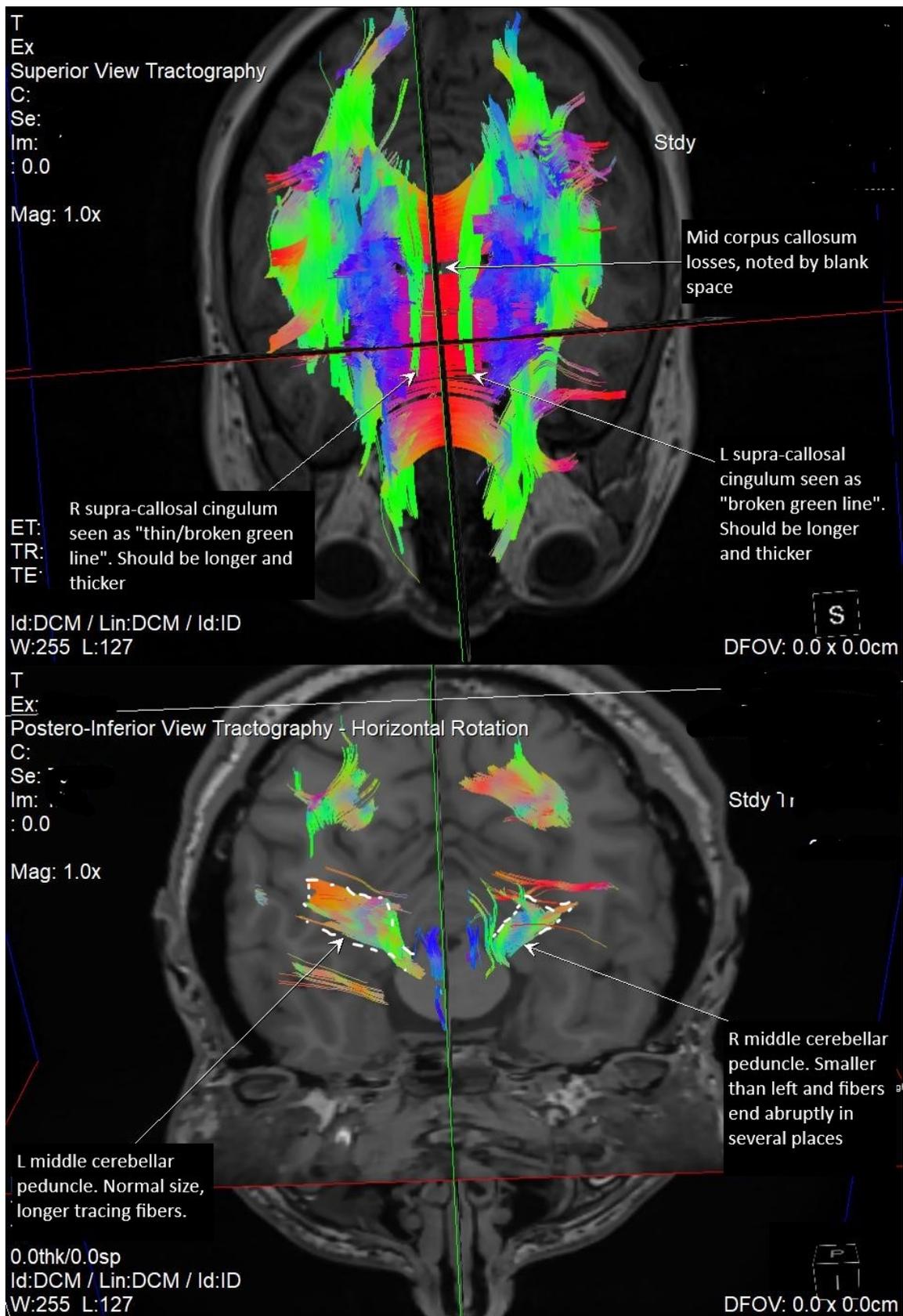


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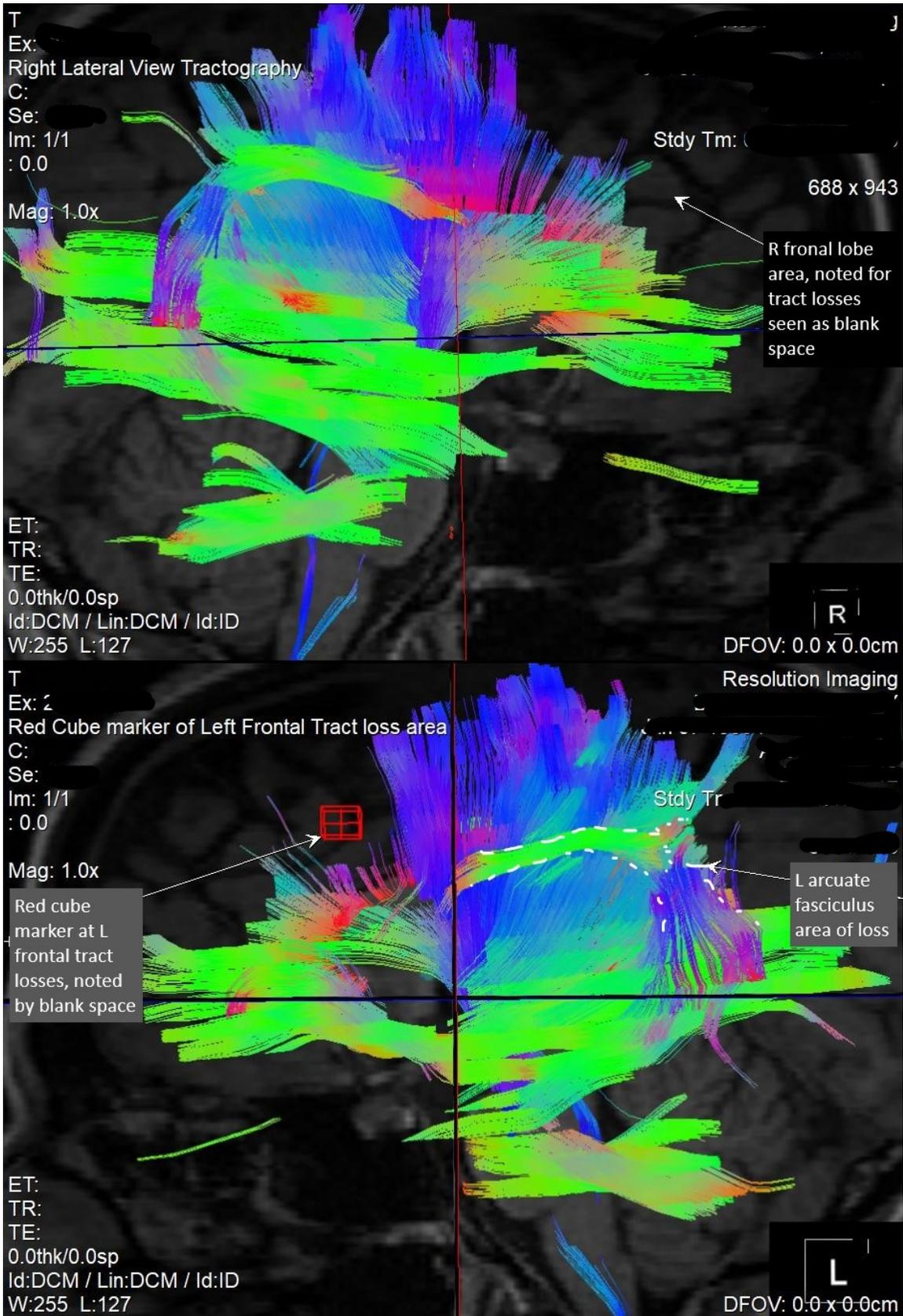


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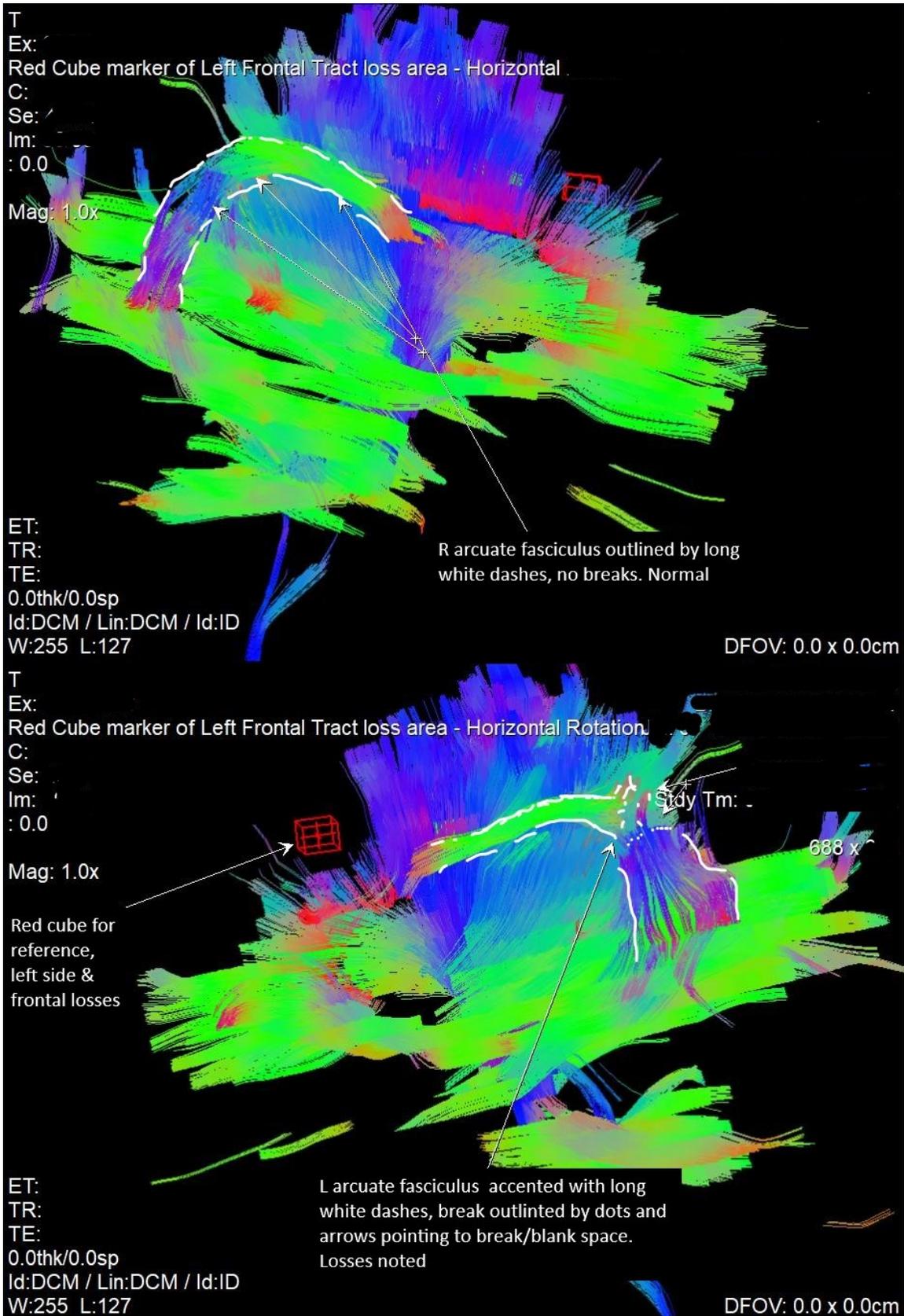


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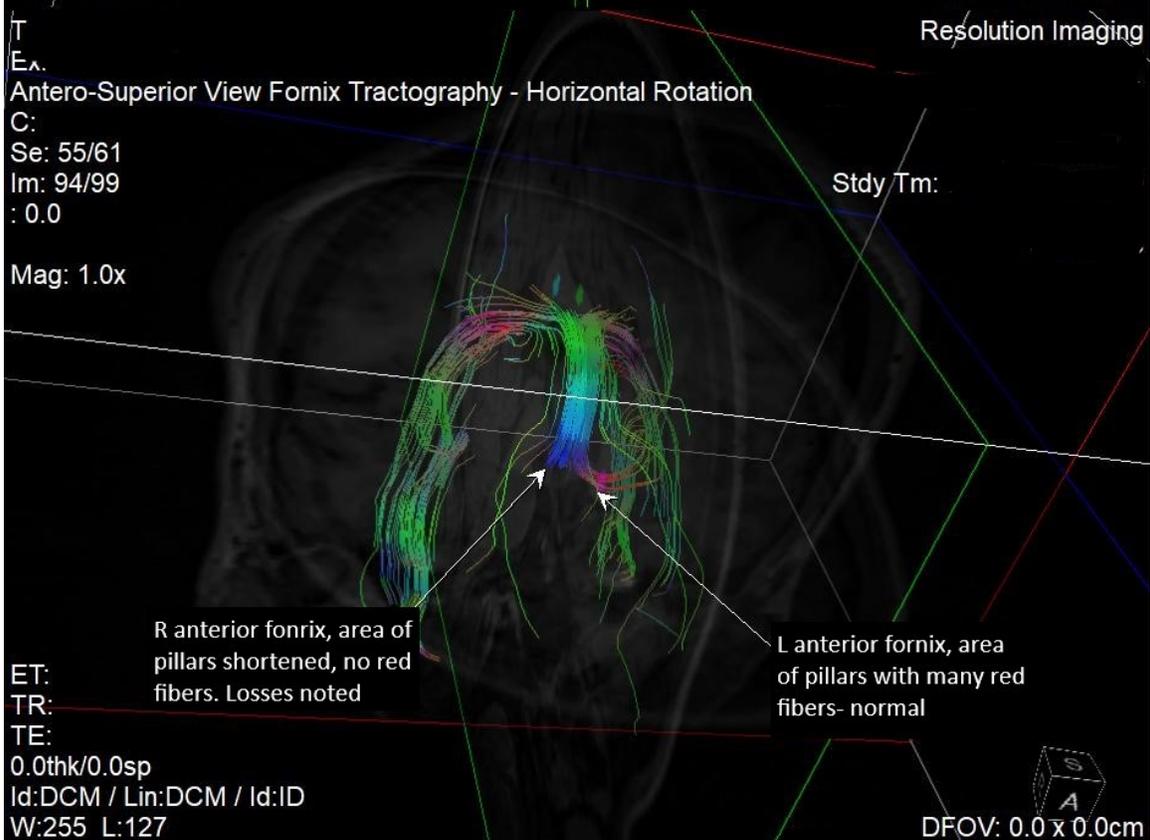
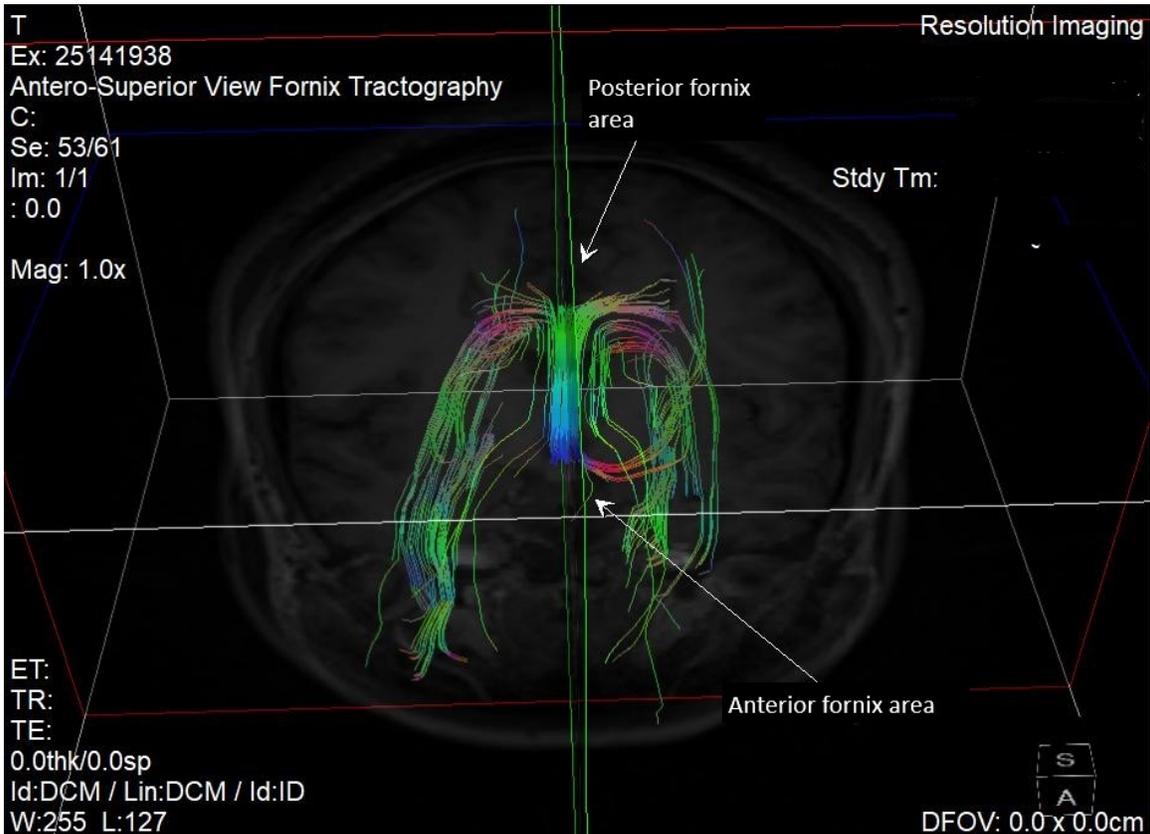


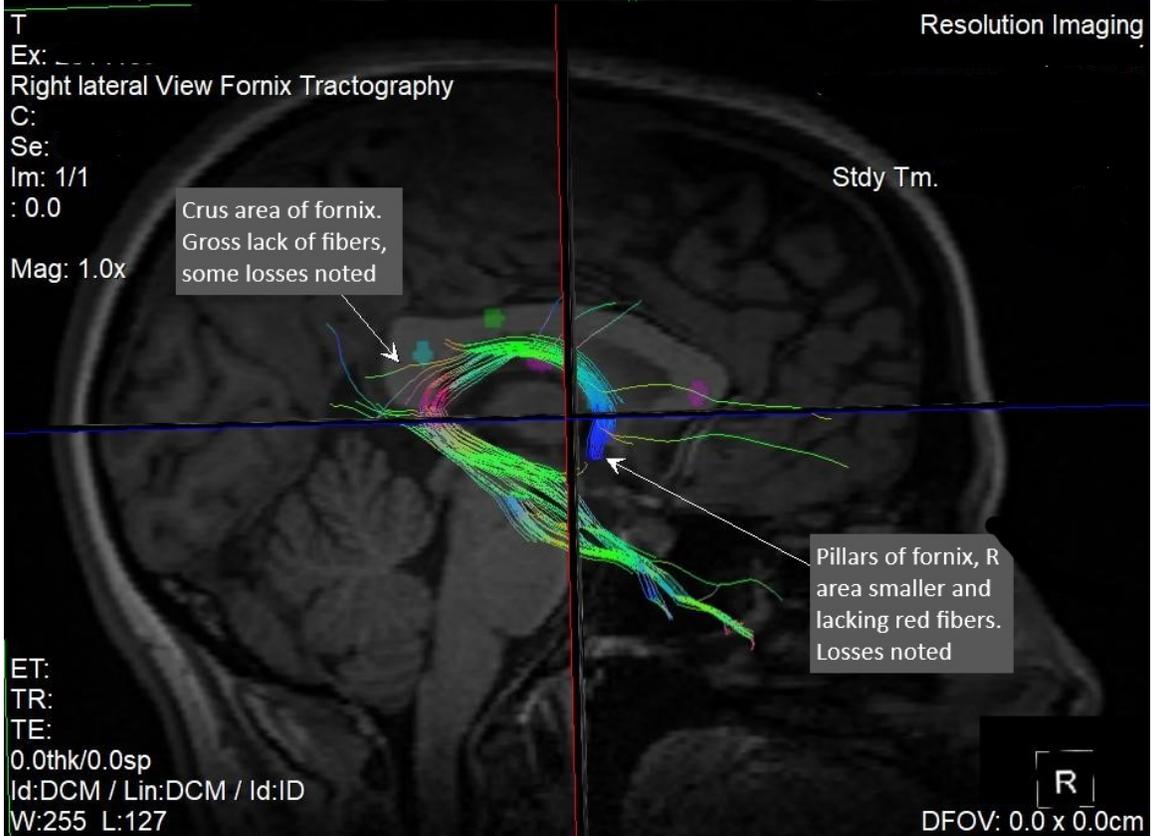
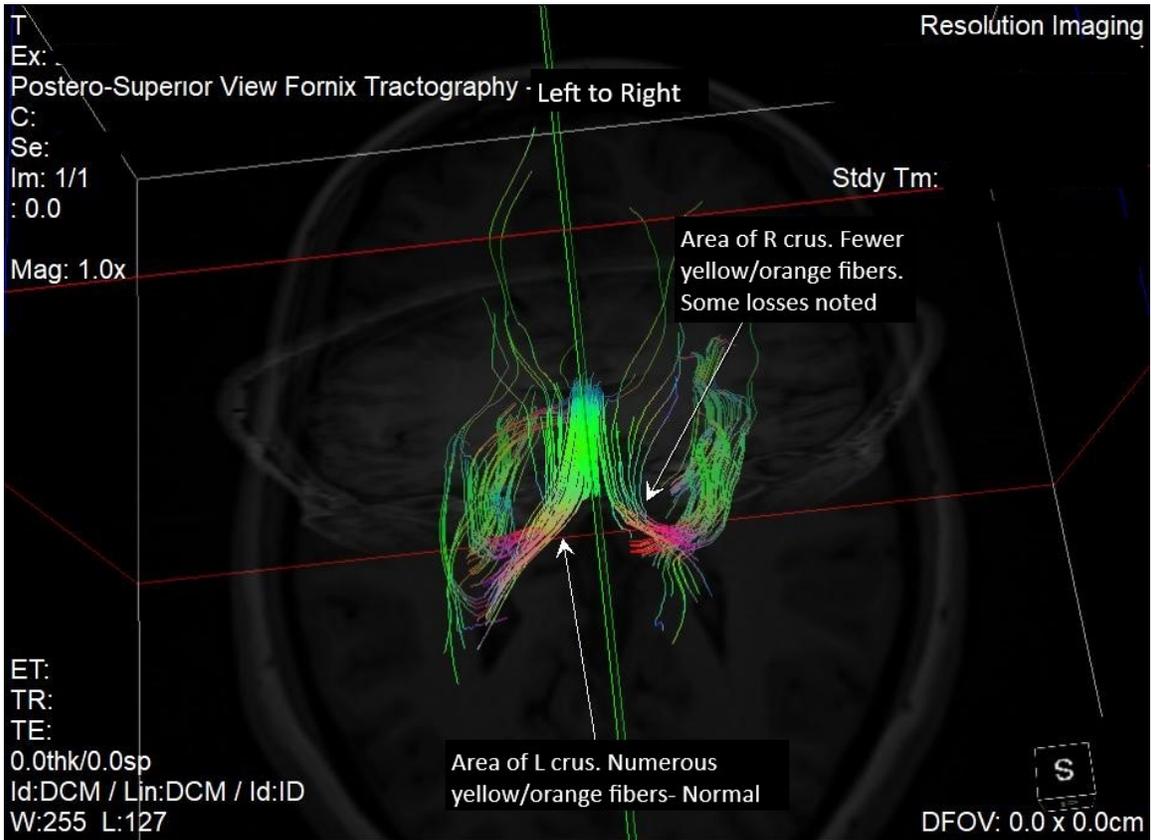
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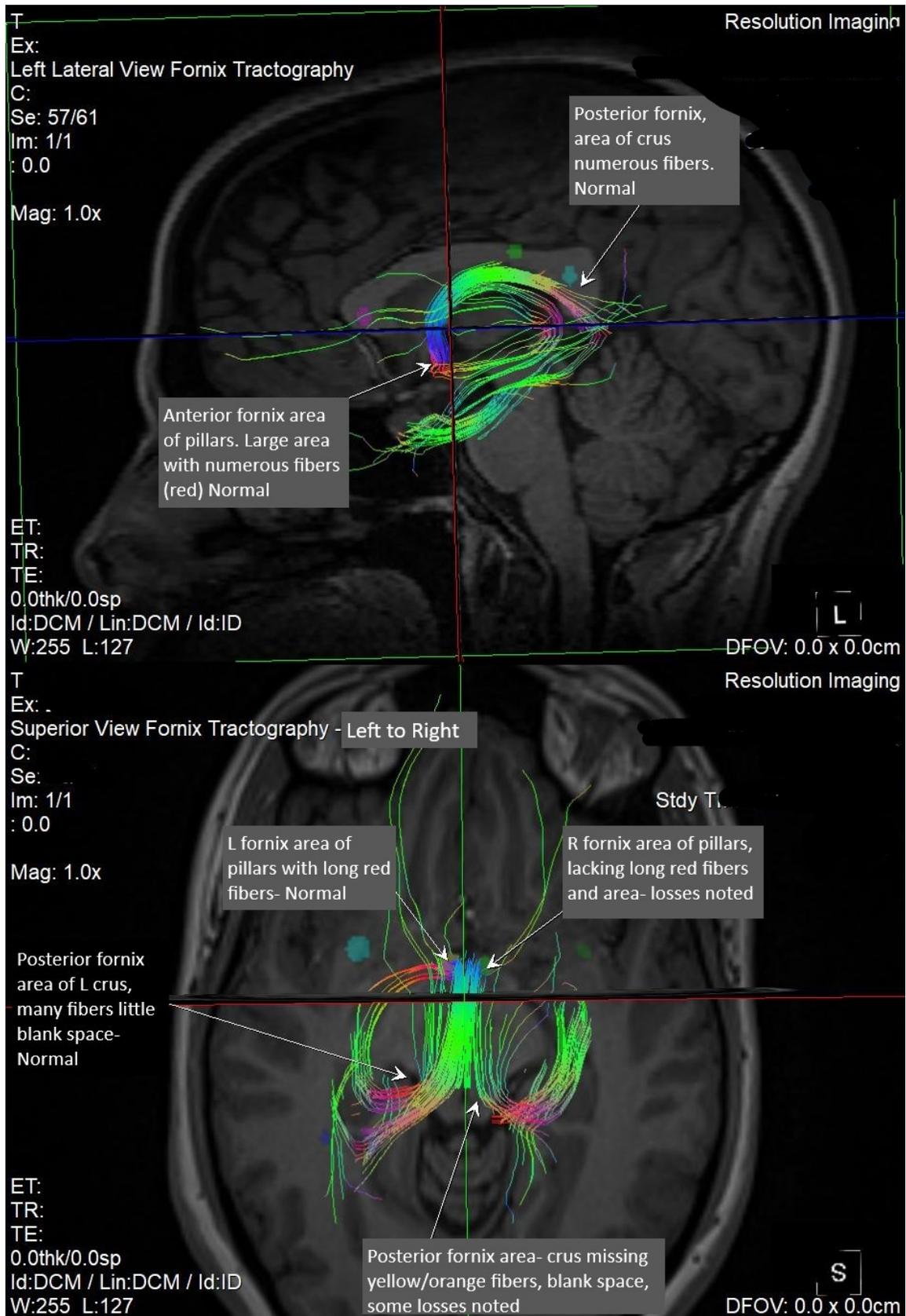


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**Routine Brain and SWI MRI FINDINGS:** These images demonstrate the brain anatomy at 3-Tesla and using a number of image sequences and image planes. The brain images are obtained in coronal, axial, and sagittal planes and include the following the coronal T2 MP GRE HEMO and or SWI sequence for micro bleeds, sagittal T2 FLAIR, axial T2 FLAIR, axial T2, axial T1 MP RAGE, coronal T2 FLAIR FS, as well as a variety of analytical evaluations including susceptibility-weighted imaging (SWI) and maximum intensity projection SWI in the coronal plane. Susceptibility weighted imaging accentuates the effect of elemental iron deposited in a brain location by bleeding or “micro-haemorrhages” in the past.

**IMAGE FINDINGS:** The routine brain MRI demonstrates relatively normal gyral-to-sulcal ratios. No evidence of atrophy. The cerebellar tonsils are normal in location. There is no mass effect or midline shift. There are no extra axial collections of fluid or blood. The sella and parasellar regions are normal. The posterior fossa is normal. The mastoid cells are clear. The sinuses and orbits are normal. There are no significant problems with the sinuses. The FLAIR imaging does not demonstrate any FLAIR abnormalities. The susceptibility-weighted imaging does not demonstrate any clear evidence of microhemorrhage.

**IMPRESSION:** Generally normal routine brain imaging. Normal FLAIR imaging. Normal susceptibility-weighted imaging. Both the fractional anisotropy and tractography analyses of the diffuser tensor imaging data demonstrate several abnormalities which include losses in the frontal lobe that can have impacts on multistep planning, map-based planning and emotional control release functions which are reflected in cognition impairment described by the patient in association with the time of the accident. Losses are appreciated in the mid-portion of the corpus callosum which is a marker for diffuse axonal injury or axonal shear injury that can have impairing effects generally on cognition; this is consistent with the patient's impairment of cognition since the time of the accident. Both studies demonstrate problems in the arcuate fasciculus which can result in impairment in speech function and this correlates with the patient's report of slurring of speech since the time of the accident. Both studies also demonstrate problems in the fornix that can result in impairment of new memory formation and this is consistent with the variety of memory formation complaints expressed by the patient with onset at the time of the accident. The tractographic analysis demonstrates losses bilaterally in the supra-callosal cingulum which is associated with depression, anxiety and does correlate with the patient's report of increased depression at the time of the accident. The fractional anisotropy and mean diffusivity analysis additionally identifies some low numbers in the hippocampal cingulum that can result in impairment of attention, which contributes to impairment of memory formation consistent with the patient's symptoms. Also, an abnormality is appreciated with an increased mean diffusivity in the basal forebrain which can be associated with sleep dysfunctions, which correlate with the patient's report of abnormal sleep function and

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insomnia, following the accident. Overall, therefore, these image findings demonstrate a number of abnormalities with expected effects on cognition, emotional function and neurologic functions as set forth in the findings above. The degree of abnormality appreciated in the imaging would be expected to result in clinically significant symptoms. The locations and types of injury are consistent with the impacts as described. Therefore, to a reasonable degree of medical certainty, it is my opinion that the abnormalities of the images seen here are a result of the trauma experienced at the time of the accident on xxxxx, and that these brain injury effects from the accident are directly causative for the symptoms as identified. Therefore, the effects of the symptoms such as problems with memory formation would be the direct result of the accident.

Signed:

A handwritten signature in black ink, appearing to read 'A. Filler', written in a cursive style.

Aaron Filler, MD, PhD

Neurography Institute Medical Associates