FAQs: VoxelBox Explore

The process- customer contacts Krishna Lal. BAI attempts to trace the root of the issue and resolve it. Be as specific as possible and if it has to be directed to someone in the BAI team, ensure it goes to only 1 poc or person who can certainly resolve the issue.

Platform, Usability, Upload, Acquisition and Product Related Questions

- 1. How does one create an account on VB explore?
 - a. Go to the <u>VB Explore website</u> and click on "Signup" to create an account.
- 2. How do I know about the series description of the modalities?

Select the series description for all modalities according to respective keywords in the dropdown list against each modality. The following modalities are mandatory:

- a. T1w: T1w, T1 Pre Contrast, T1, Ax T1 Bravo, Sag T1 Bravo, 3D T1, etc.
- b. rs-fMRI: fMRI, resting fMRI, rest fMRI, resting state, rest, rs-fMRI, rs fmri, etc.
- c. FLAIR: flair, ax flair, sag flair, 3D flair, dark-fluid, etc.
- d. DTI/dMRI: dwi, dmri, diffusion, diffusion-weighted, diffusion mri, DMRI high ISO, etc.
- 3. If the above doesn't work, who do I contact to figure out the right series description?
 - a. Please contact Sachin Patalasingh
- 4. How do I know if an upload has been completed?

You will receive an email after your upload is successful or if it has failed due to network errors.

5. Where is my voxelbox ID?

Your VoxelBox ID for each patient is a combination of 4 numbers unique to your account, a hyphen and 4 numbers of the patient ID you assign. This number can often be found when you receive the confirmation email of having uploaded a dataset. It can also be found in the URL of the report for that patient. For example, if the ID for your account is 0123, and you upload a case with the ID 9999, the VoxelBox ID for that patient is 0123-9999.

6. Can I use my patient's UHID for uploading data?

We recommend NOT to use any component of your patient's UHID to protect the patient's privacy as per regulations. You can use any unique 4-digit identifier to upload data.

7. How can I view my results?

There are three ways which can be used to view results:

- a. Click on the "Report" icon on the patient's tab to open our dynamic report for a quick view of your results.
- b. Click on the "View" icon on the patient's tab to open BrainSightAl's proprietary viewer to get a detailed view of the images.
- c. Click on "Download results" to save your processed images as DICOM and NIFTI files. They can be opened on any viewer of your choice.

8. The reports are really slow to load. Once loaded, switching to different networks or tracts takes a lot of time.

Clear cache, cookies, and browsing history. Then reload the page

9. Why is the download button for some of my cases not active?

a. The download button will be activated once the internal review by the BrainSightAl team is done.

10. How to write the data on CD/DVD from PACS/ Console/ Workstation?

- a. There are two ways to write/burn the data on CD/DVD:
 - i. Download the files to your local system and then burn the CD/DVD
 - Write/Burn the CD/DVD directly from PACS/ Console/ Workstation in standard medium. Avoid writing/copying the data in Patient Medium/Factory Medium

11. Shall we anonymise the data before uploading it on VBExplore?

- a. No, we do not recommend anonymising the data because if the data is anonymised, then the results will also be anonymised. Anonymised results cannot be used in Neuronavigation with other images.
 - i. In case you want to use anonymised results in neuronavigation, you have to use our base/structural image only as underlay for our results

12. Can you integrate VoxelBox into our system/PACS so that we can transfer the data seamlessly?

a. Please coordinate with our software team

13. Will any resting state or diffusion sequence work?

a. No. We recommend acquiring the data with our set protocol only; otherwise, it would not be processable by us.

14. Will any FLAIR or T1W sequence work?

a. No. We recommend acquiring the data with our set protocol only; otherwise, it would not be processable by us

15. The BrainSight protocols are taking a lot of MR Time. Can you reduce it?

- a. BrainSight follows a very high standard MR acquisition protocol that has been optimised for time as well as quality. The standard protocol takes around 20-30 minutes, comprising 3D T1W, 3D FLAIR, 160 dynamics resting-state fMRI at TR <= 2.9s, and B0,B1000 weighted diffusion images at maximum direction.</p>
- b. If your machine is 1.5T, the time might increase by an additional 10-15 minutes.
- c. If you want to reduce the time, please contact Sachin Patalasingh

16. We are facing trouble acquiring MR as the patient is moving and not cooperating. Can you acquire the scans under anaesthesia?

a. No, we do not recommend acquiring the scans under anaesthesia as it will affect the results

Data Processing Related Questions, outputs failing etc, why we cannot process it

17. What should I do if I receive an email that my processing failed? (or) whom do I contact for support if anything fails?

Go to the Vbexplore platform to the failed screen. Click on "Contact support" -> you can dial the number displayed on the screen. You can also send your queries to support@brainsightai.com and we will help you at the earliest.

About VB and the Outputs

18. How have you validated your results?

We have benchmarked our rs-fMRI pipeline against tb-fMRI -> rs-fMRI vs tb-fMRI study report:

https://docs.google.com/document/d/1myocEJDNUywKQWIP2LWcVQBmcuKfyf-uKrCtciF55f E/edit#heading=h.4kbr8g7otvny; Lateralization Study Report:

 $\underline{https://docs.google.com/document/d/1nUYPi9cqh7gjn8HzD8txbrfDTh6wlay5lzDsdn0Vtvc/editheading=h.4kbr8g7otvny}.$

For dMRI study report:

https://docs.google.com/document/d/1GyuOV3IYUETMQY_MRyREz7IALQKxhab5Xtl9mGg DsNw/edit?usp=sharing Further, BrainSight has built guardrails for each of these processes which checks for discrepancies or possible errors made in the analysis at different levels due to technical limitations. There are two layers of guardrails:

1. Processing Guardrail: This guardrail checks for inaccuracies in the fMRI and dMRI preprocessing for a subject based on the following criteria:

a. fMRI:

- i. Skull-Stripping: Skull-Stripping/Brain Extraction is one of the most important steps in neuroimaging analysis as it extracts the brain and removes skull-related information from the image which leads to accurate registration of images and overall analysis. If the guardrail flags this as an error, it means that the skull-stripping has not been performed with the highest possible accuracy for a subject which can lead to further errors in the analysis.
- ii. Coregistration with Anatomical Image: Coregistration with Anatomical Image ensures that the fMRI is properly aligned with the reference image spatially. If the guardrail flags this as an error, it means that the coregistration has not been performed optimally which can cause further errors in registration processes and atlas based analysis.
- iii. **Normalization:** Normalization of fMRI is done to transform the fMRI into a standard space which enables faster and accurate atlas based analysis. If the guardrail flags this as an error, it means that the normalization process has not been performed optimally which can further errors in registration of atlases and corresponding analysis.

b. dMRI:

- i. **Skull-Stripping:** This process removes the skull and other non-brain tissues from diffusion-weighted imaging (DWI) scans, ensuring accurate brain extraction. If an error is flagged, it indicates that the skull-stripping was not performed accurately, potentially leading to further errors in image registration and analysis.
- ii. Coregistration with Anatomical Image: This step aligns the Fiber Orientation Distribution (FOD) with the ACPC-corrected T1 image. An error flag here indicates suboptimal coregistration, which can cause inaccuracies in subsequent registration processes and atlas-based analyses.
- iii. **Quality of FOD:** This checks the quality of the FOD image. If flagged, it means the FOD image quality is poor, affecting the accuracy of tractography results.

2. Output Guardrail

a. fMRI:

i. Hyper-Parameter Optimisation/Personalisation: Every human brain is different and the signals acquired can vary due to several factors like MR Machine, Software version, Acquisition Parameters, etc. This guardrail guarantees that the best hyper-parameters for Denoising of rs-fMRI and other analysis are used for the subject. If the guardrail flags this as a failure, we will be unable to personalise hyper-parameters for the subject it means at the moment.

- **ii. Spurious Activations:** This guardrail ensures that there are no spurious activations that lie outside the brain area. If this fails, we will be unable to remove the spurious activations for a given subject at the moment.
- iii. Atlas Registration & Masking: This guardrail ensures that the atlas registration and masking is done optimally to perform the network extraction process at highest possible accuracy. This guardrail flags even the slightest error in terms of masking and related registration, which we will be unable to optimise for the given subject at the moment.

b. dMRI:

- i. **Extra Fibers:** This checks for the presence of streamlines belonging to a different bundle.
- ii. **ACT Score:** This evaluates whether streamlines end in anatomically accurate regions. A low ACT score indicates that streamlines terminate incorrectly, impacting tract quality.

BrainSight is committed to providing the best possible results to the user. If you notice any discrepancies or if the guardrail renders the subject as not processable for you, please provide us the feedback which will help us improve our AI to correct these errors.

19. How is language laterality calculated?

Language Laterality is analyzed using a method called "Dynamic Lateralization Index" which captures dynamic changes in laterality over time using a sliding window approach. We use the SENSAAS atlas (SENT_CORE) to parcellate the denoised rs-fMRI to derive a time-series of ROIs present in the SENSAAS atlas. We would have a voxel time series for each ROI (for both L & R hemispheres individually: Ex: L_stg, R_stg, etc.). The rs-fMRI global signal data (L & R separately), ROI data (L & R separately) is divided into shorter time windows, and connectivity analysis is performed separately for each window. For each window, the connectivity correlation is calculated between the ROI data and global signal (for respective hemispheres) with application of Fisher R to Z over the same, and standard application of Laterality Index (LI) formula is applied: LI = (L - R) / (L + R). This results in LI for each window from the rs-fMRI. Finally, the mean value of LI of all windows is taken into account to determine the final LI: 0.15 to 1.0 = Left; -0.15 to 0.15 = Bi-Lateral; -0.15 to 1.0 = Right. Link to Paper:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8929635/#:~:text=Specifically%2C%20we%2 Oinvestigated%20the%20laterality,fMRI%20data%20from%20the%20Human

20. Why are there activations on Tumor/Lesion?

The denoising of rs-fMRI requires White Matter, and CerebroSpinal Fluid Segmentation maps to remove confounding signals based on these anatomical components and motion related noise. These segmentation maps are derived from the T1w image which sometimes contain the lesion/tumor of the same intensity as grey matter or any other tissues which reduces the effect of denoising. To combat this our pipeline supports T1w and T2-FLAIR included segmentation to denoise better and also using lesion/tumor masks which can be derived from T1w, T2-FLAIR, and T1Ce structural modalities. We recommend thresholding

the networks appropriately or ignoring the spurious activations over the tumor while we are working towards this inherent imaging limitation.

21. Why are there fibers on Tumor/Lesion?

The DWI image used for generating FOD image is in a lower resolution compared to structural image which can cause fibers to encroach the lesion/tumor boundary. Tumor/lesions having similar intensity to grey matter can cause encroachment as well.

22. What do FA, MD, AD, Cs, Cp etc mean?

These diffusion MRI metrics (FA, MD, AD, RD, linearity, planarity, sphericity) assess the integrity and organization of white matter tracts, aiding in the diagnosis of neurological conditions.

- 1. **Fractional Anisotropy (FA)**: Measures the directionality of water diffusion. High FA indicates aligned fiber tracts in white matter.
- 2. **Mean Diffusivity (MD)**: Average rate of water diffusion. High MD suggests tissue degeneration or increased extracellular space.
- 3. **Axial Diffusivity (AD)**: Diffusion along the main axis of fibers. Changes can indicate axonal damage.
- 4. **Radial Diffusivity (RD)**: Diffusion perpendicular to the main axis. Increased RD suggests demyelination.
- 5. **Linearity**: Reflects diffusion along a single direction, indicating organized fiber tracts.
- 6. **Planarity**: Indicates diffusion in a plane, seen in areas where fibers fan out or intersect.
- 7. **Sphericity**: Measures diffusion in all directions, typical in less organized tissues like gray matter.

23. How to interpret rs-fMRI results?

In the report, there will be a colorbar attached in "hot" colorscale which represents red/black as hypo activations and yellow/white as hyper activations.



24. How to interpret tractography results?

The report includes a tri-colored directional legend in the top right corner, using the standard red-green-blue (RGB) code to represent the spatial locations of terminal regions of each pathway. The color coding convention is as follows:

- Red: Represents transverse fibers (commissural tracts) connecting one hemisphere to the other, indicating directions along the X axis (right to left or left to right).
- Green: Represents anteroposterior direction fibers (association tracts), indicating directions along the Y axis (posterior to anterior or anterior to posterior).
- Blue: Represents craniocaudal fibers (projection tracts) connecting the cerebral cortex with caudal structures (subcortical centers, brainstem, and spinal cord), indicating directions along the Z axis (foot-to-head or head-to-foot).



25. How is tractography performed?

After generating FOD(Fiber Orientation Distribution) image from DWI(Diffusion Weighted Imaging) image, our tractography algorithm reconstructs streamlines using white matter rois as starting seeds and performs anatomically constrained probabilistic tracking.

26. How are networks derived from rs-fMRI?

The networks are derived using Independent Component Analysis (ICA) which are then compared with personalised network templates derived from the Human Connectome Project's atlas.

27. Under what conditions does the tractography process fail?/Why did my tractography process fail?

BrainSight has built guardrails for each of these processes which checks for discrepancies or possible errors made in the analysis at different levels due to technical limitations. There are two layers of guardrails:

Processing Guardrail:

- **Skull-Stripping:** This process removes the skull and other non-brain tissues from diffusion-weighted imaging (DWI) scans, ensuring accurate brain extraction. If an error is flagged, it indicates that the skull-stripping was not performed accurately, potentially leading to further errors in image registration and analysis.
- Coregistration with Anatomical Image: This step aligns the Fiber Orientation
 Distribution (FOD) with the ACPC-corrected T1 image. An error flag here indicates
 suboptimal coregistration, which can cause inaccuracies in subsequent registration
 processes and atlas-based analyses.
- Quality of FOD: This checks the quality of the FOD image. If flagged, it means the FOD image quality is poor, affecting the accuracy of tractography results.

Output Guardrail:

- Extra Fibers: This checks for the presence of streamlines belonging to a different bundle.
- ACT Score: This evaluates whether streamlines end in anatomically accurate regions. A low ACT score indicates that streamlines terminate incorrectly, impacting tract quality.

28. Under what conditions does the network mapping process fail?/Why did my network mapping process fail?

BrainSight has built guardrails for each of these processes which checks for discrepancies or possible errors made in the analysis at different levels due to technical limitations. There are two layers of guardrails:

3. **Processing Guardrail:** This guardrail checks for inaccuracies in the fMRI preprocessing for a subject based on the following criteria:

a. fMRI:

- i. Skull-Stripping: Skull-Stripping/Brain Extraction is one of the most important steps in neuroimaging analysis as it extracts the brain and removes skull-related information from the image which leads to accurate registration of images and overall analysis. If the guardrail flags this as an error, it means that the skull-stripping has not been performed with the highest possible accuracy for a subject which can lead to further errors in the analysis.
- ii. Coregistration with Anatomical Image: Coregistration with Anatomical Image ensures that the fMRI is properly aligned with the reference image spatially. If the guardrail flags this as an error, it means that the coregistration has not been performed optimally which can cause further errors in registration processes and atlas based analysis.
- iii. **Normalization:** Normalization of fMRI is done to transform the fMRI into a standard space which enables faster and accurate atlas based analysis. If the guardrail flags this as an error, it means that the normalization process has not been performed optimally which can further errors in registration of atlases and corresponding analysis.
- **4. Output Guardrail:** This guardrail checks for inaccuracies in the fMRI network mapping analysis for a subject based on the following criteria:

a. fMRI:

- i. Hyper-Parameter Optimisation/Personalisation: Every human brain is different and the signals acquired can vary due to several factors like MR Machine, Software version, Acquisition Parameters, etc. This guardrail guarantees that the best hyper-parameters for Denoising of rs-fMRI and other analysis are used for the subject. If the guardrail flags this as a failure, we will be unable to personalise hyper-parameters for the subject it means at the moment.
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which we will be unable to optimise for the given subject at the moment.

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29. How will the data be used for AI?

The pseudonymised imaging data and feedback on the outputs will be used to improve the performance of the AI system by annotations, textual inputs, manual/automated labelling without any use of PHI. The improvement areas would be as follows:

- a. Skull-Stripping/Brain Extraction
- b. Registration
- c. Atlas Registration
- d. Network Mapping <> Independent Component Analysis
- e. Tractography Correction
- f. Lesion/Tumor Segmentation
- g. Tissue Segmentation
- h. Tagging and categorization of imaging data on cloud/datalake
- i. Lateralization of Networks
- j. Guardrails to ensure safe and accurate outputs are given to the user

30. There are so many files in the results, and I don't know what to use for neuronavigation.

- a. The neuronavigation files are present in a folder with the prefix "Neuronav"
- b. If you have Medtronic S8, you can use Neuronav_Fused; for other Medtronic systems, you can use Neuronav_Mask
- c. The Viewer files can only be used on nifti viewers like MRView and MRICroGL

31. How to use results on Neuronavigation?

a. Please refer to the Neuronavigation documentation for more information

Admin + Finance + Billing + Legal stuff

32. What is the cost of our product?

33. Can I use my patient's UHID for uploading data?

We recommend NOT to use any component of your patient's UHID to protect the patient's privacy as per regulations. You can use any unique 4-digit identifier to upload data.

34. How is my patient's data protected?

- a. All patient data is stored on secured cloud based/local servers.
- b. Hospitals can share data through our secure cloud based platform VB explore

- c. At BrainsightAl data undergoes automated processing, data is handled by team members only by limited teams and specific purposes such as review and quality checks of results, research or product development etc.
- d. Patient data is used for any model training or research purposes only after anonymization by ABC steps.
- 35. What is our PAN and GST Number for billing purpose?
- 36. About the company and the founders and the team there is a pdf for this.
- 37. About our investors please direct this query to the sales team.
- 38. About our studies available on the website.
- 39. About our customers please direct this query to sales team.
- 40. What is the status of my case?

Other

These Should come on top

What formats are the results shared in

Can I load results in the neuronavigations system? Yes. We support what all -> Follow up to that

Some questions on radiology reporting? Can show

How much does it take to get results? Approx 10 hours (before surgery time) -> approved indications

For rehab - > we will have to discuss and get back (e.g., TMH is taking 2-3)

How do I view the results? -> talk about MR viewer (dynamic), load results and view during surgery

Validation of the results?

How is language laterality calculated?