NeuroLens: A Novel Live Surgical Aid for Brain Tumor Removal using Augmented Reality and Deep Learning

Problem

- ❖ The anatomy of the brain, in particular the extraordinarily **fragile and vital structures** that function in cohesion, serves as the primary cause for the **diminished survival rate** associated with **brain cancer** (Syed, 2022).
- ❖ Outcomes for patients are similarly adverse; the **5-year survival rate** for brain cancer is only **36%**.
- ❖ Critical structures, such as **blood vessels** and **white matter**, often **interfere with surgical removal**, necessitating utmost precision and care when operating throughout the brain.
  - ➢ This issue is heightened by the fact that the actual **locations of these critical structures** are **not readily available** from the perspective of the surgical site.
  - ➢ Surgeons have to consistently **switch perspectives** between the surgical site and the **2D preoperative scans**, diverting their focus away from the operation and possibly **further endangering critical anatomical structures**.

2D Preoperative Scans

Image from Children's Hospital of Philadelphia

- ❖ Furthermore, current neuronavigation systems can be costly, and may subject patients to excess radiation
- ❖ Such challenges can contribute to **several complications** during brain tumor resection procedures including:
  - ➢ Changes in motor, sensory, and speech function
  - ➢ Bleeding, aneurysms, and possibly strokes
  - ➢ Partial tumor removal and post-operative complications

Background Research

Limitations of Current Neuronavigation

- ❖ The only information surgeons currently utilize is scan data from magnetic Resonance Imaging (MRI), Computed Tomography (CT), etc. displayed on separate 2D monitors. However, **delineating tumors, vasculature, and nervous boundaries from 2D images in the three-dimensional context of the surgical site can be extraordinarily difficult**, and additional pressure is placed on the surgeon.
- ❖ Limited spatial and 3D information is derived directly from the 2D scans and due to the changing nature of anatomical structures and complex tumor shapes from patient to patient, **each operation** is akin to **navigating a completely different environment** from a sole planar perspective.
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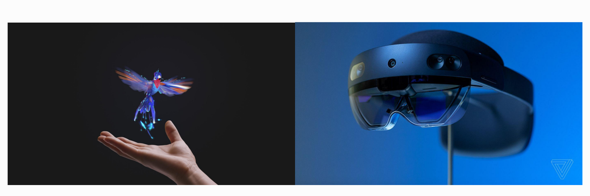
Augmented Reality in Brain Tumor Removal

- ❖ Evidently, a system and methodology are required for the **visualization of these critical anatomical structures** in a location that is in view of the surgical site and in **three dimensions**.
- ❖ The concept of **augmented reality (AR)** can be applied towards this specific purpose, to provide the surgeon with a comprehensive view of necessary anatomical structures directly on the patient. AR allows for the combination of virtual elements with a real-world view.
  - ➢ Thus, this technology preserves the observation of the surgical site through the surgeon's perspective, while overlaying virtual elements and data necessary to ensure safer tumor resection.



Augmented Reality and Hololens 2

- ❖ This novel technology applied to the purpose of brain tumor resection would be unprecedented in its field. With AR, the **3D nature of the tumor, vasculature, and nervous tracts can be visualized** in real-time on the patient, akin to a surgeon having **X-ray vision**.
- ❖ This comprehensive view can be expanded to include **all information necessary for the surgery**, including medical scans, detailed 3D models of anatomy, and the ability to conduct intraoperative monitoring.
- ❖ A dynamic surgical aid able to **superimpose the tumor** onto the patient in **exactly the right position** and deliver data to the surgeon in real-time has the potential to significantly **improve the risk of harming critical structures** and the ability to completely remove the tumor.

Hypothetical AR Use in Surgery

Research Objectives

The present project provides an **AR system** that transforms unlabeled 3D medical scans such as Magnetic Resonance Imaging (MRI) outputs into a comprehensive visualization of the tumor, vasculature, and white matter tracts in AR during tumor resection surgeries. The system employs both **deep learning** and **augmented reality**.

Goal 1: Anatomical Segmentation

A **deep learning** model, using a 3D U-NET, was programmed and trained to automatically segment **brain tumors** in 3D from MRIs. A second deep learning model utilizing the RE-NET algorithm was constructed to segment **cerebral vasculature** from MRAs. An algorithm was constructed to identify **white matter tracts** from diffusion tensor imaging volume utilizing a Deterministic Maximum Direction Getter.

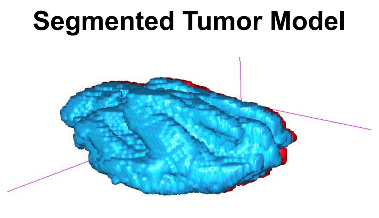
Goal 2: Hololens 2 AR Application

The patient-specific 3D models were then implemented in Unity, uploaded to the **Hololens 2**, and superimposed in real-time onto a physical simulator head utilizing an unprecedented **6DOF tracking algorithm**. This surgical aid provides three other AR visualization modes to further assist users, and features to ensure ease-of-use and adaptability in the surgical environment.

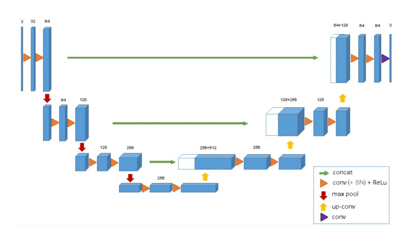
Engineering Methodology

Tumor and Vascular Segmentation

Deep Learning Segmented Tumor Model



3D U-NET Architecture



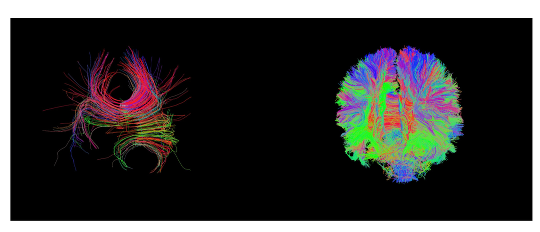
The previous year's project developed **deep learning models** for the segmentation, or outlining, of brain tumors and cerebral vasculature.

- ❖ A **3D U-NET**, an **encoder-decoder architecture** designed for volumetric medical segmentation, was constructed to delineate the exact boundaries of tumors from preoperative 3D MRIs.
- ❖ Cerebrovascular segmentation was facilitated through the design of a **Reverse Edge Attention Network** specifically for identifying tubelike structures from Magnetic Resonance Angiographies (MRA).
- ❖ Patient-specific models obtained for the intention of visualization in AR.

White Matter Tractography

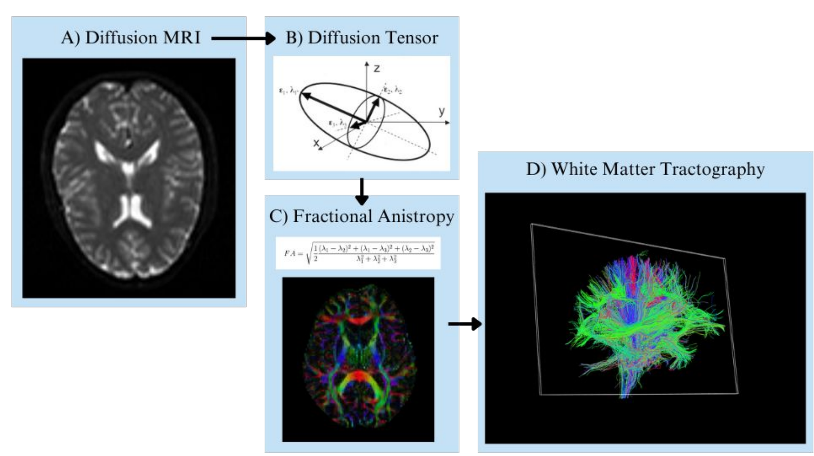
White matter tractography is a three-dimensional modeling technique employed for the **visualization of nerve tracts** obtained through diffusion MRI. These models could play an important role, particularly in the removal of brain tumors, as they aid in **preserving functional connectivity around essential nerve pathways** and providing insights into potential obstructions, thereby minimizing the risk of neurological damage.

- ❖ At each voxel of the diffusion MRI, water diffusion is recorded, encompassing both direction and magnitude measurements.
- ❖ The **Deterministic Maximum Direction Getter (DMDG)** algorithm is employed to generate multiple modalities of tractography, extracting optimal information. Eigenvalues and eigenvectors corresponding to each diffusion tensor are computed to convert the diffusion MRI into an operable format.
- ❖ The **fractional anisotropy**, a quantifiable metric of the degree of diffusion, is calculated for every diffusion tensor. White matter tracts, characterized by anisotropic diffusion influenced by the myelin sheath barrier, exhibit higher fractional anisotropy values in contrast to lower values indicative of isotropic diffusion.



Generated Tractography (Full Brain and Corpus Callosum

Diffusion MRI to Tractography Workflow

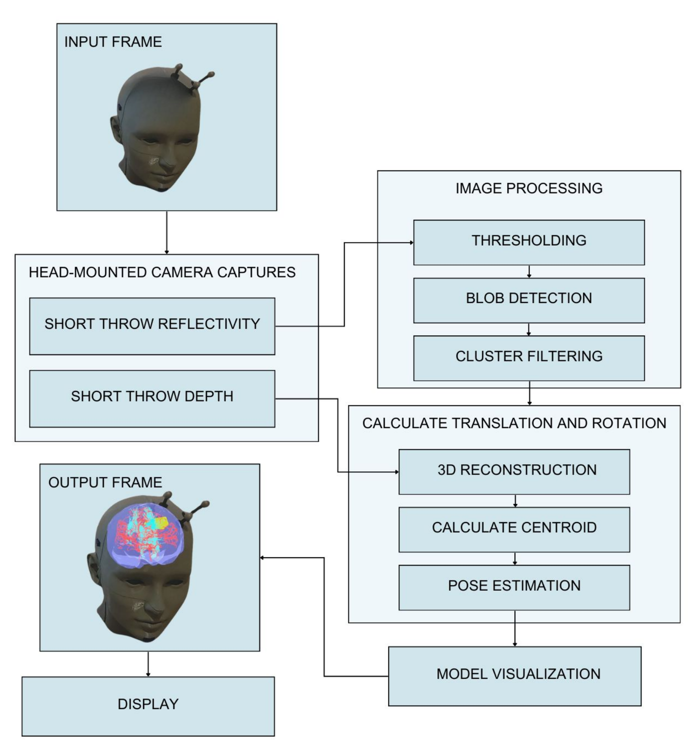


- ❖ Seed points are selected through a uniform predefined procedure referencing anatomical landmarks, and tracts are mapped through the most probable pathways.
- ❖ The outcome is a bundle of streamlines representing the white matter tractogram, formatted in a vector-based structure compatible with widely used 3D visualization software.
- ❖ For the streamlines to be visualized in augmented reality, they must have volume, resulting in the creation of tubes characterized by three edges and vertices at 15-degree or greater angle changes along the streamlines. This optimization is necessary for enhancing model performance in the augmented reality environment.

Retroreflective Marker Tracking

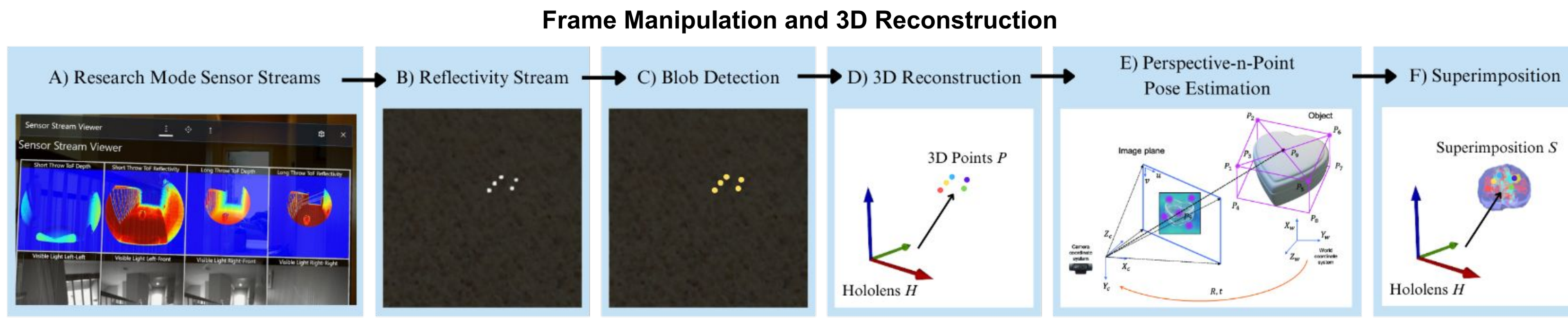
A system was programmed into the NeuroLens application for the **6 DoF real-time tracking of a phantom patient head** through the use of **retroreflective markers**, and deployed onto the Hololens 2. These markers, necessary for the tracking system, exhibit a spherical retroreflective design, causing emitted light rays to reflect back in the same direction toward the source.

- ❖ The **Hololens 2 has four cameras**: a two Time of Flight (ToF) sensors (Near/Far) and two RGB stereo cameras (Left/Right)
- ❖ The tracking algorithm developed for this system harnesses the two output frames of the near ToF sensor—**short throw reflectivity (str) and short throw depth (std)**—to create a three-dimensional reconstruction of the retroreflective markers.
- ❖ The operational flow initiates with a request for two frames from the near ToF depth sensor, converted into operable two-dimensional arrays. Markers appear especially bright in the str frame.
- ❖ The str frame is normalized such that zero represents no reflectivity and one represents maximum reflectivity. A threshold was used to binarize the array.
- ❖ **Clusters are identified through a blob detection algorithm**, accompanied by a test for similar sizes. Pixel radius measurements aid in determining the presence of clusters with similar radii, while unusually small lone clusters, potentially indicative of camera lens interference, are filtered out. The remaining clusters undergo a circularity test through the isoperimetric quotient.

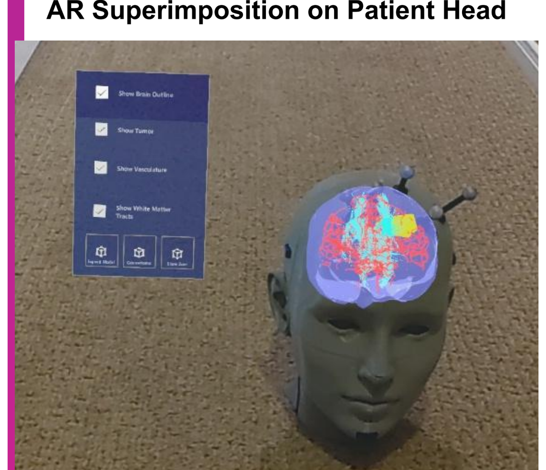


Marker Tracking Process Flowchart

Frame Manipulation and 3D Reconstruction



AR Superimposition on Patient Head



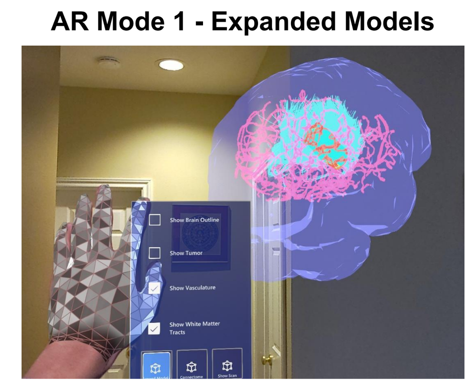
- ❖ In instances of marker overlap from a specific orientation, clusters are omitted, given that reconstruction remains achievable from the remaining markers. These recorded clusters are subsequently mapped to the output frame std, facilitating 3D reconstruction of the markers.
- ❖ The **centroid of the markers** serves as the pivotal point for superimposing anatomical models. To calculate the orientation for full 6 DoF tracking, a **pose estimation algorithm** is implemented, identifying translation and rotation. The centroid is converted to a translation vector relative to the camera, and using the **Perspective-n-Point** pose estimation algorithm, a **rotation matrix is derived from the 3D positions** of the markers and the thresholded str stream.
- ❖ **Anatomical models are then superimposed** on the patient phantom head based on the translation vector and rotation matrix, augmented by a constant scale and additional translation to account for the cameras' offsets in calibration.

Surgical Application Modes and Features

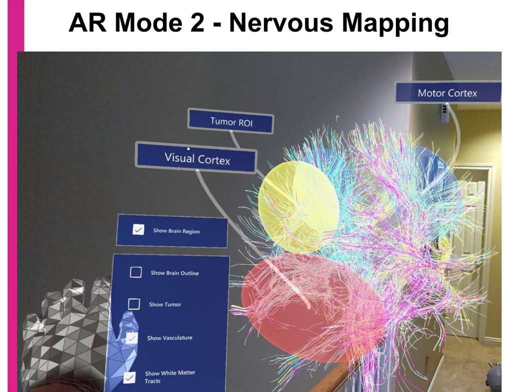
Mode 1

The first mode entails the **enlargement of anatomical models** to a scale of the user's preference, detaching these models from the constraints of the patient's head size. This enlargement is particularly advantageous for preoperative planning and analysis, enabling a more detailed examination of visual intricacies.

AR Mode 1 - Expanded Models



AR Mode 2 - Nervous Mapping



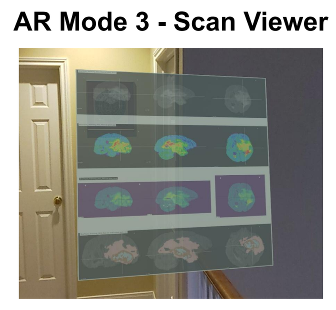
Mode 2

The second mode is an augmented reality implementation of the neurosurgical procedure known as **Intraoperative Neurophysiological Monitoring (IONM)**. Functional mapping of the nerves within the brain is **vital to understanding patient responses** when dealing with tumors **near critical areas of brain function**, especially subcortical pathways. Utilizing patient-specific DTI, the various tractograms are visualized in a dynamic interface for a comprehensive understanding of nervous mapping. These visualizations - the white matter tractography and full connectome - can be selectively shown through the usage of the button panel. The connectome is rendered in color according to nervous structures such as motor control, sensory processing, language processing, and higher-order capabilities such as cognition, emotion, and connation.

Mode 3

The third modality facilitates the **visualization of medical scans** in three dimensions during surgery, eliminating the need for the user to switch between the surgical site and external 2-dimensional screens. This AR presentation maintains visual consistency with external screens, yet it unfolds in real-world space. Compatible scans, including but not limited to MRI, MRA, computed tomography (CT), and DTI, can be visualized using two distinct methods: the rendering of a single pivotal slice, or the rendering of any slice through a slider interface in the lower left corner of the visualization.

AR Mode 3 - Scan Viewer



Spatial Mapping

The head-mounted display device incorporates several sensors to **mitigate any perceptible jitter** in airborne holograms. Upon application initiation, the NeurolLens scans the user's surroundings, creating a geometric reconstruction through sensor data and **Simultaneous Localization and Mapping (SLAM)**.

Spatial anchors emerge as a pivotal facet of NeuroLens' function, expanding on the spatial mapping by tethering holograms and virtual elements to any point within the 3D map.

Spatial Mapping

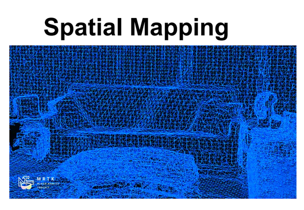


Image from Microsoft Learn MRTK 2

Hand and Eye Tracking

NeuroLens utilizes user hand and eye movements to facilitate natural and seamless interaction with holograms and other virtual elements. Hand gestures allow users to interact with the surgical holograms and use the button panel. The eye tracking functions through user-specific calibration ensuring properly fitted visualizations.

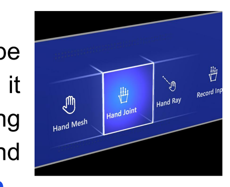
Hand Joint Tracking

The surgical aid utilizes this through **hands-free processes**, allowing **gaze and voice** to control the application.

User Experience (UX)

A user-friendly **graphical interface**, specifically tailored for seamless operation during surgical procedures, is implemented in the application. This button panel is equipped with 3D colliders, and **senses finger contact** with the virtual button using hand tracking.

The user interface can be interacted with as if it were physical, mimicking standard procedure and maximizing **ease of use**.



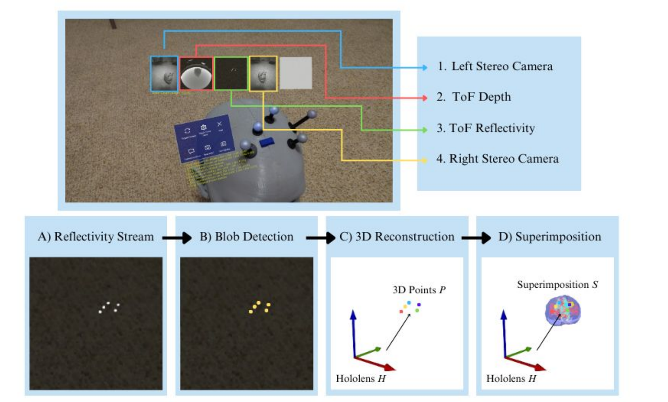
3D Button Panel

Results

The **evaluation** of the surgical aid was based upon the **performance of several sub-systems**, each implemented with the intent to address a specific issue of the tumor resection operation.

Tracking Accuracy

The tracking system was evaluated at certain stages of processing, from the initial marker detection to the final supe

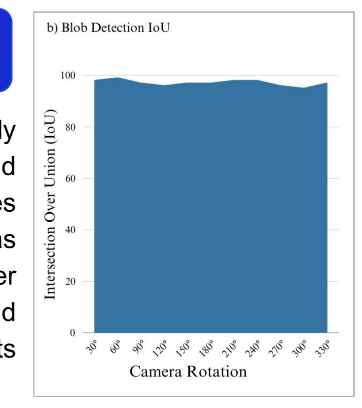


Marker Tracking Process Evaluation

Four main stages of the tracking algorithm are identified: the **initial reflectivity stream, blob detection, 3D reconstruction, and finally superimposition.**

Blob Detection Accuracy: 98%

The ability of the surgical aid to fully capture the extent of the marker and filter out other reflective surfaces such as lenses and screens was measured with Intersection over Union (IoU) at each position around the phantom head achieving results of 96% and 99% accuracy.



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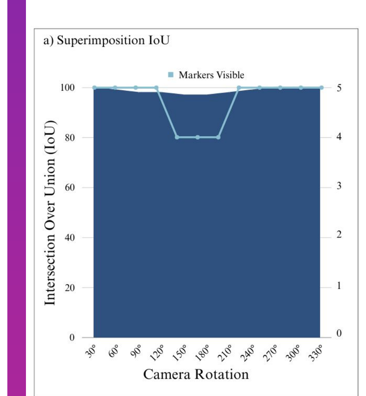


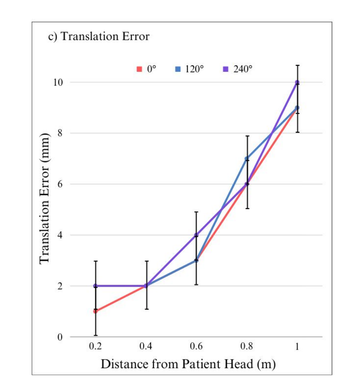
Superimposition IoU

Superimposition Accuracy: 98%

Evaluation at the superimposition stage (D), followed a similar pattern. The intersection of the virtual model and the physical head boundaries were measured with IoUs between 97 and 100 percent, signifying NeuroLens' ability to perform 6DOF tracking.

Translation Error: 2 mm

Finally, the translation error, computed in millimeters, was tested against the distance of the Hololens from the patient phantom. Errors reached as low as 2 mm at a distance of 0.2 m from the patient phantom.



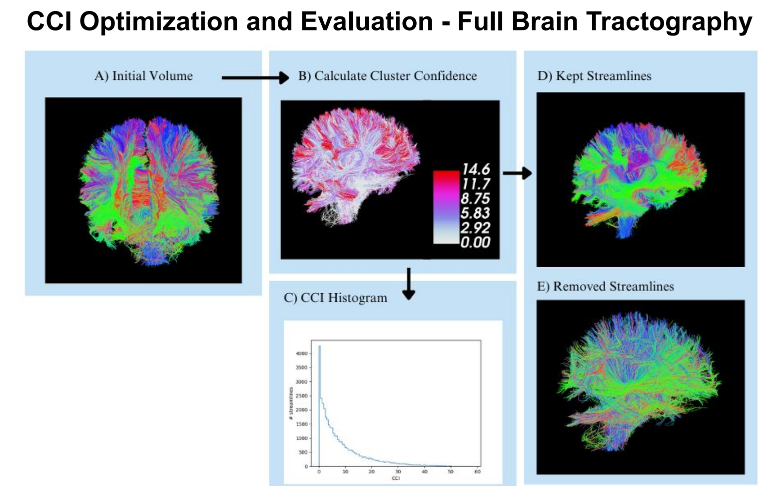
Translation Error

White Matter Tractography Accuracy

A method of evaluation and optimization for white matter tractography was implemented, the **Cluster Confidence Index (CCI)**.

- ❖ The CCI, an outlier scoring methodology, compares and scores streamlines based on other streamlines with similar pathways
- ❖ Filters out lone streamlines and prioritize higher confidences
- ❖ Evaluates the accuracy of the tractography

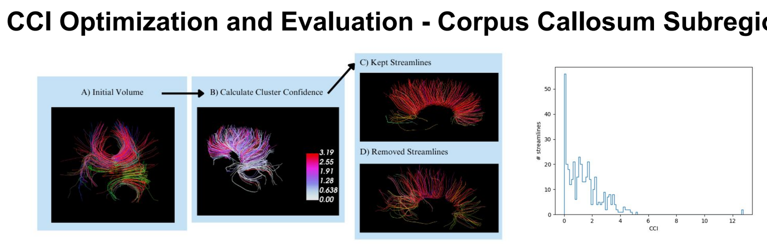
CCI Optimization and Evaluation - Full Brain Tractography



(a) Initial tractogram obtained through DMDG algorithm. (b) Evaluation of CCI for each streamline. (c) Histogram depicting CCI for every streamline. (d) Streamlines with Cluster Confidence Index of greater than 1 are retained. (e) Outliers that were omitted from D are visualized

The figure shows that only 5% of the streamlines had CCIs of one or less, signifying a high degree of accuracy.

CCI Optimization and Evaluation - Corpus Callosum Subregion



Conclusions and Next Steps

- ❖ **Brain cancer** has one of the **lowest survival rates** due to the fragility of the brain and the proliferation of tumors into critical structures.
  - ➢ Surgical removal of these tumors necessitates extraordinary precision, yet surgeons' sole guide is a separate 2D screen.
- ❖ This project develops an **AR live surgical aid** using the Hololens 2, providing 3D comprehensive data directly onto the surgical site.
  - ➢ The surgical aid possesses a **tracking algorithm** to recognize a patient's head through retroreflective markers, a system to delineate **tumor, vasculature, and nervous boundaries** and superimpose them onto the patient's head, **three additional modalities** to readily provide necessary data, and a **comprehensive UX equipped with voice recognition** for ease of use.
- ❖ Evaluation of the systems employed in the surgical aid revealed **astoundingly accurate segmentation, detection, and superimposition.**
- ❖ Further work on this project will include implementing:
  - ➢ Machine learning in the white matter tractography system
  - ➢ Adding features to the surgical aid such as a visualization of the surgical path.
- ❖ The applications for this live surgical aid are widespread, from the intended use of intraoperative aid to medical training, preoperative planning, and assistance to other surgical operations.

In conclusion, NeuroLens has the potential to **revolutionize brain surgery** and **significantly improve surgical outcomes for millions of patients.**

All photos, images, and graphics were made by the researcher unless otherwise stated.

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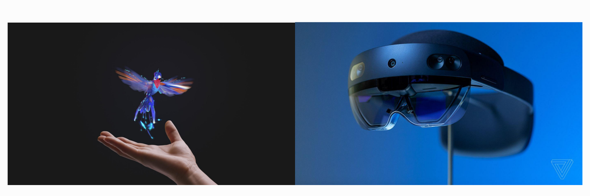

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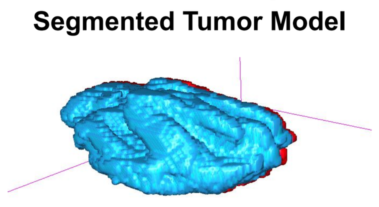
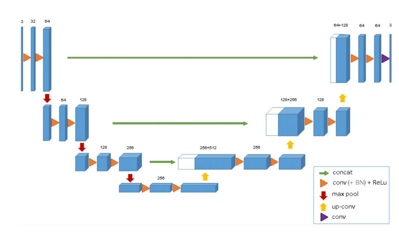
Engineering Methodology

Tumor and Vascular Segmentation

Deep Learning Segmented Tumor Model



3D U-NET Architecture



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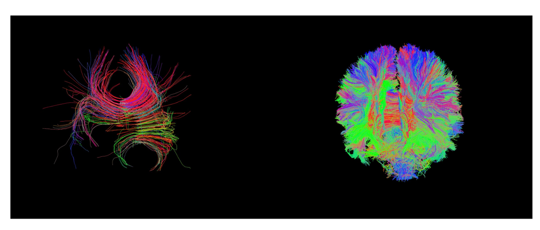
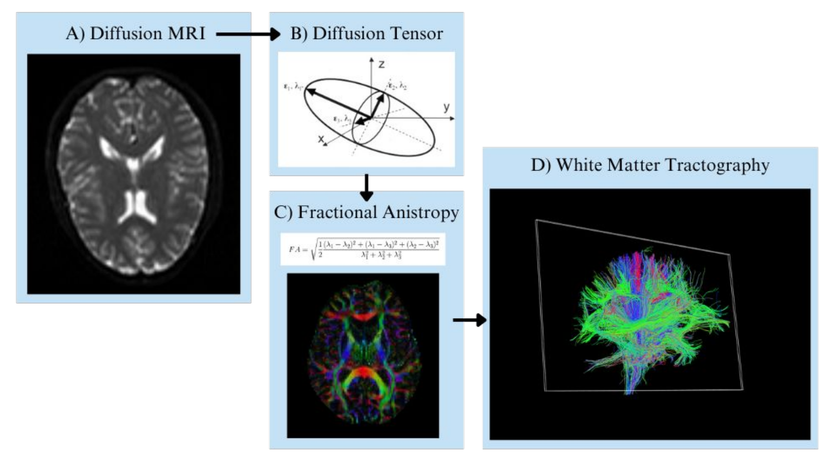


Generated Tractography (Full Brain and Corpus Callosum)

Diffusion MRI to Tractography Workflow



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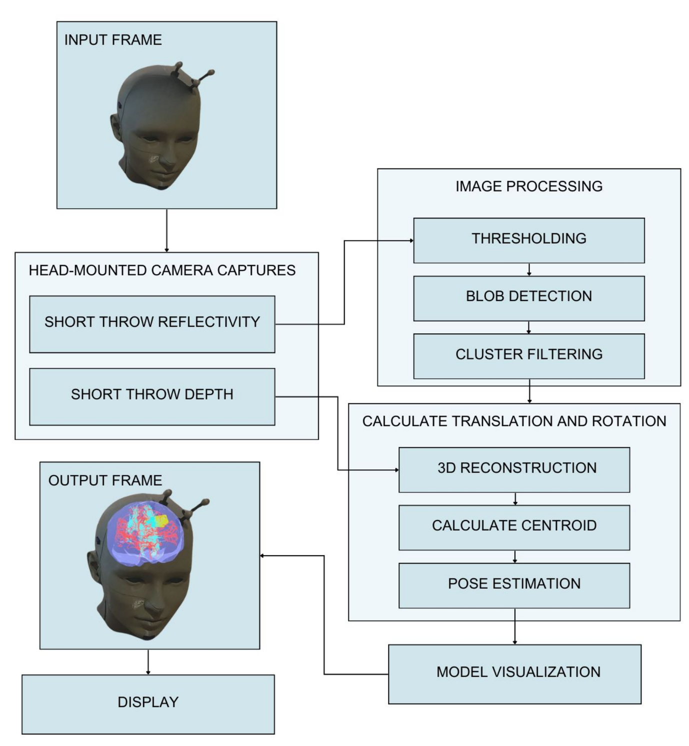
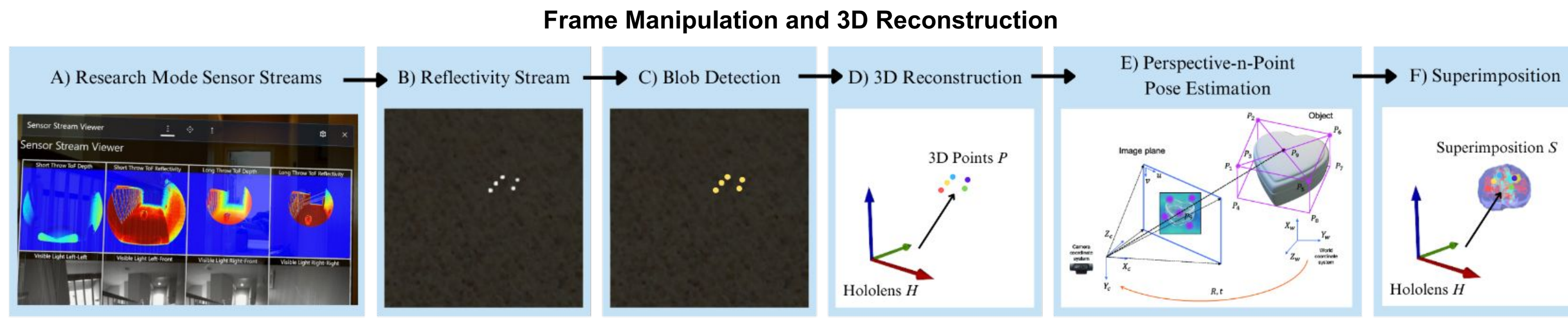
A system was programmed into the NeuroLens application for the **6 DoF real-time tracking of a phantom patient head** through the use of **retroreflective markers**, and deployed onto the Hololens 2. These markers, necessary for the tracking system, exhibit a spherical retroreflective design, causing emitted light rays to reflect back in the same direction toward the source.

- The **Hololens 2 has four cameras**: a two Time of Flight (ToF) sensors (Near/Far) and two RGB stereo cameras (Left/Right)
- The tracking algorithm developed for this system harnesses the two output frames of the near ToF sensor—**short throw reflectivity (str) and short throw depth (std)**—to create a three-dimensional reconstruction of the retroreflective markers.
- The operational flow initiates with a request for two frames from the near ToF depth sensor, converted into operable two-dimensional arrays. Markers appear especially bright in the str frame.
- The str frame is normalized such that zero represents no reflectivity and one represents maximum reflectivity. A threshold was used to binarize the array.
- **Clusters are identified through a blob detection algorithm**, accompanied by a test for similar sizes. Pixel radius measurements aid in determining the presence of clusters with similar radii, while unusually small lone clusters, potentially indicative of camera lens interference, are filtered out. The remaining clusters undergo a circularity test through the isoperimetric quotient.

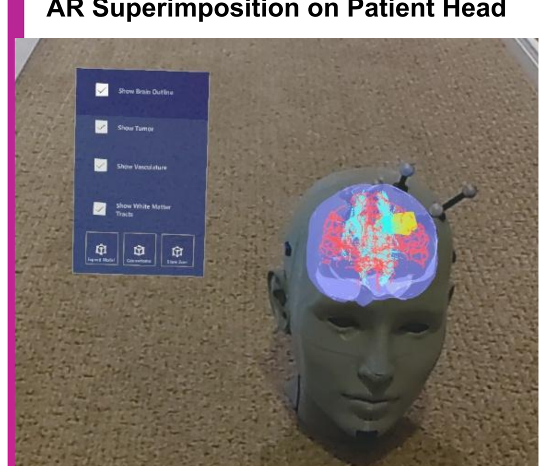


Marker Tracking Process Flowchart

Frame Manipulation and 3D Reconstruction



AR Superimposition on Patient Head



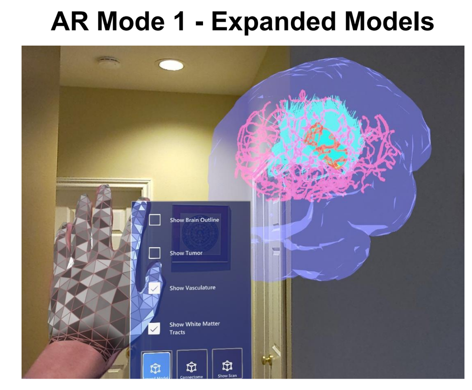
- In instances of marker overlap from a specific orientation, clusters are omitted, given that reconstruction remains achievable from the remaining markers. These recorded clusters are subsequently mapped to the output frame std, facilitating 3D reconstruction of the markers.
- The **centroid of the markers** serves as the pivotal point for superimposing anatomical models. To calculate the orientation for full 6 DoF tracking, a **pose estimation algorithm** is implemented, identifying translation and rotation. The centroid is converted to a translation vector relative to the camera, and using the **Perspective-n-Point** pose estimation algorithm, a **rotation matrix is derived from the 3D positions** of the markers and the thresholded str stream.
- **Anatomical models are then superimposed** on the patient phantom head based on the translation vector and rotation matrix, augmented by a constant scale and additional translation to account for the cameras' offsets in calibration.

Surgical Application Modes and Features

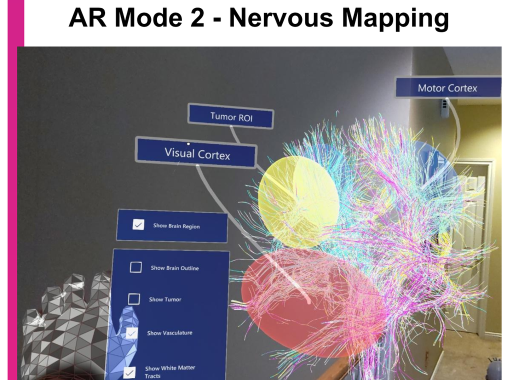
Mode 1

The first mode entails the **enlargement of anatomical models** to a scale of the user's preference, detaching these models from the constraints of the patient's head size. This enlargement is particularly advantageous for preoperative planning and analysis, enabling a more detailed examination of visual intricacies.

AR Mode 1 - Expanded Models



AR Mode 2 - Nervous Mapping



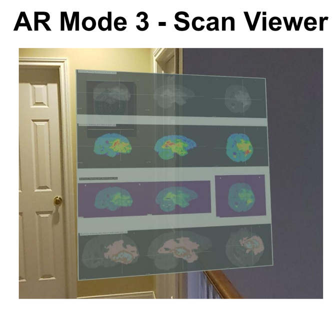
Mode 2

The second mode is an augmented reality implementation of the neurosurgical procedure known as **Intraoperative Neurophysiological Monitoring (IONM)**. Functional mapping of the nerves within the brain is **vital to understanding patient responses** when dealing with tumors **near critical areas of brain function**, especially subcortical pathways. Utilizing patient-specific DTI, the various tractograms are visualized in a dynamic interface for a comprehensive understanding of nervous mapping. These visualizations - the white matter tractography and full connectome - can be selectively shown through the usage of the button panel. The connectome is rendered in color according to nervous structures such as motor control, sensory processing, language processing, and higher-order capabilities such as cognition, emotion, and conation.

Mode 3

The third modality facilitates the **visualization of medical scans** in three dimensions during surgery, eliminating the need for the user to switch between the surgical site and external 2-dimensional screens. This AR presentation maintains visual consistency with external screens, yet it unfolds in real-world space. Compatible scans, including but not limited to MRI, MRA, computed tomography (CT), and DTI, can be visualized using two distinct methods: the rendering of a single pivotal slice, or the rendering of any slice through a slider interface in the lower left corner of the visualization.

AR Mode 3 - Scan Viewer



Spatial Mapping

The head-mounted display device incorporates several sensors to **mitigate any perceptible jitter** in airborne holograms. Upon application initiation, the NeuroLens scans the user's surroundings, creating a geometric reconstruction through sensor data and **Simultaneous Localization and Mapping (SLAM).**

Spatial Mapping

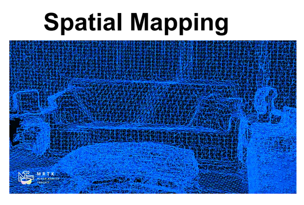


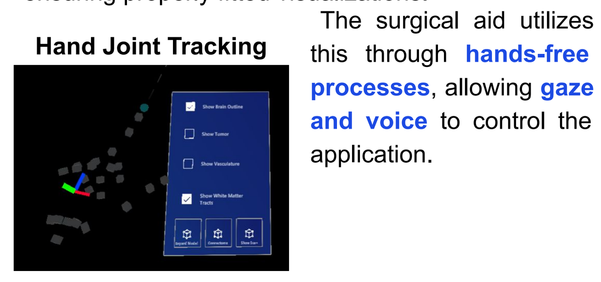
Image from Microsoft Learn MRTK 2

Spatial anchors emerge as a pivotal facet of NeuroLens' function, expanding on the spatial mapping by tethering holograms and virtual elements to any point within the 3D map.

Hand and Eye Tracking

NeuroLens utilizes user hand and eye movements to facilitate natural and seamless interaction with holograms and other virtual elements. Hand gestures allow users to interact with the surgical holograms and use the button panel. The eye tracking functions through user-specific calibration ensuring properly fitted visualizations.

Hand Joint Tracking

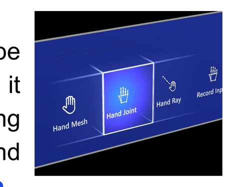


The surgical aid utilizes this through **hands-free processes**, allowing **gaze** and **voice** to control the application.

User Experience (UX)

A user-friendly **graphical interface**, specifically tailored for seamless operation during surgical procedures, is implemented in the application. This button panel is equipped with 3D colliders, and **senses finger contact** with the virtual button using hand tracking.

The user interface can be interacted with as if it were physical, mimicking standard procedure and maximizing **ease of use**.



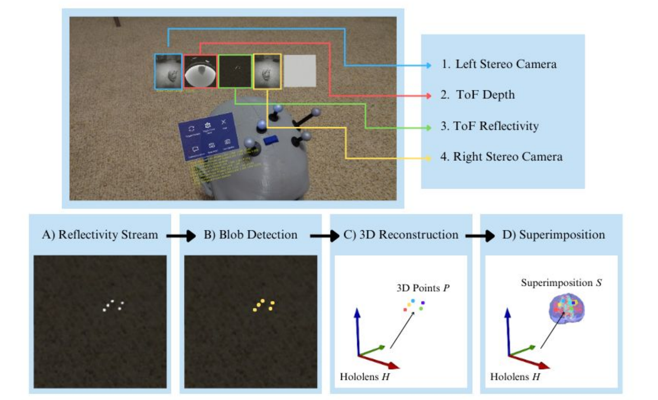
3D Button Panel

Results

The **evaluation** of the surgical aid was based upon the **performance of several sub-systems**, each implemented with the intent to address a specific issue of the tumor resection operation.

Tracking Accuracy

The tracking system was evaluated at certain stages of processing, from the initial marker detection to the final supe

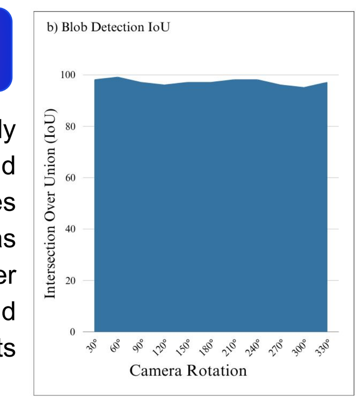


Marker Tracking Process Evaluation

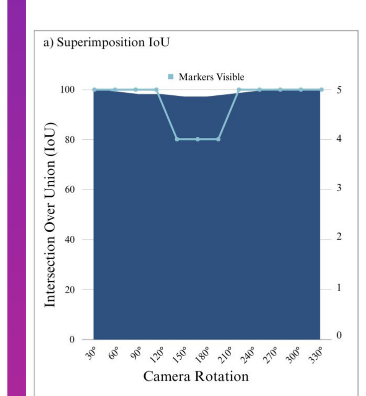
Four main stages of the tracking algorithm are identified: the **initial reflectivity stream, blob detection, 3D reconstruction, and finally superimposition.**

Blob Detection Accuracy: 98%

The ability of the surgical aid to fully capture the extent of the marker and filter out other reflective surfaces such as lenses and screens was measured with Intersection over Union (IoU) at each position around the phantom head achieving results of 96% and 99% accuracy.



Blob Detection IoU



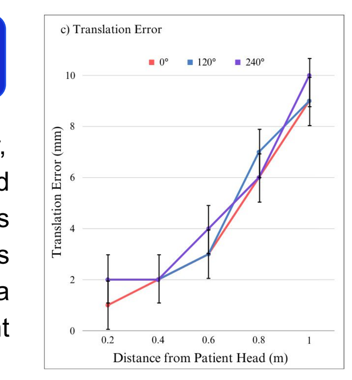
Superimposition IoU

Superimposition Accuracy: 98%

Evaluation at the superimposition stage (D), followed a similar pattern. The intersection of the virtual model and the physical head boundaries were measured with IoUs between 97 and 100 percent, signifying NeuroLens' ability to perform 6DOF tracking.

Translation Error: 2 mm

Finally, the translation error, computed in millimeters, was tested against the distance of the Hololens from the patient phantom. Errors reached as low as 2 mm at a distance of 0.2 m from the patient phantom.



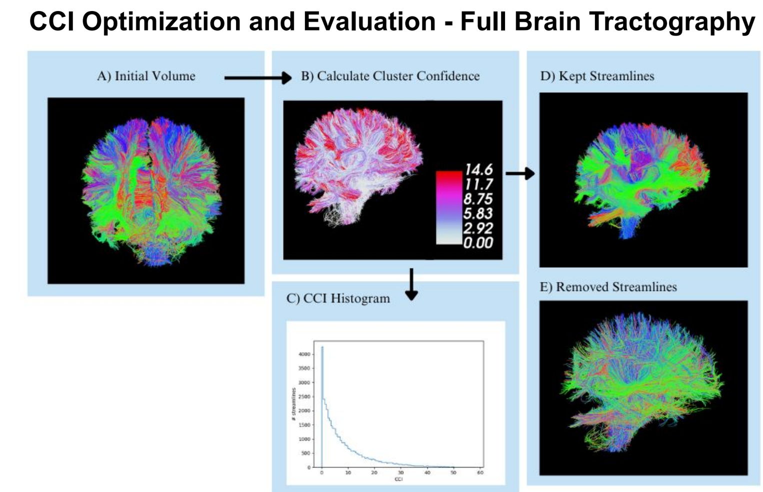
Translation Error

White Matter Tractography Accuracy

A method of evaluation and optimization for white matter tractography was implemented, the **Cluster Confidence Index (CCI)**.

- The CCI, an outlier scoring methodology, compares and scores streamlines based on other streamlines with similar pathways
- Filters out lone streamlines and prioritize higher confidences
- Evaluates the accuracy of the tractography

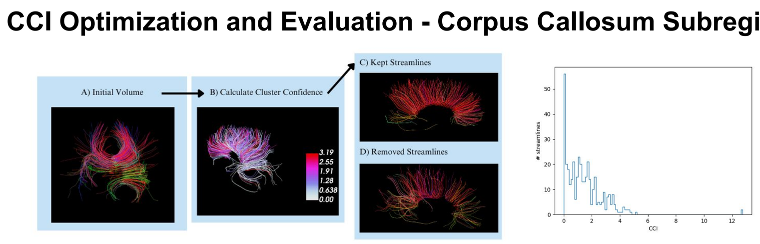
CCI Optimization and Evaluation - Full Brain Tractography



(a) Initial tractogram obtained through DMDG algorithm. (b) Evaluation of CCI for each streamline. (c) Histogram depicting CCI for every streamline. (d) Streamlines with Cluster Confidence Index of greater than 1 are retained. (e) Outliers that were omitted from D are visualized

The figure shows that only 5% of the streamlines had CCIs of one or less, signifying a high degree of accuracy.

CCI Optimization and Evaluation - Corpus Callosum Subregion



Conclusions and Next Steps

- **Brain cancer** has one of the **lowest survival rates** due to the fragility of the brain and the proliferation of tumors into critical structures.
  - Surgical removal of these tumors necessitates extraordinary precision, yet surgeons' sole guide is a separate 2D screen.
- This project develops an **AR live surgical aid** using the Hololens 2, providing 3D comprehensive data directly onto the surgical site.
  - The surgical aid possesses a **tracking algorithm** to recognize a patient's head through retroreflective markers, a system to delineate **tumors, vasculature, and nervous boundaries** and superimpose them onto the patient's head, **three additional modalities** to readily provide necessary data, and a **comprehensive UX equipped with voice recognition** for ease of use.
- Evaluation of the systems employed in the surgical aid revealed **astoundingly accurate segmentation, detection, and superimposition.**
- Further work on this project will include implementing:
  - Machine learning in the white matter tractography system
  - Adding features to the surgical aid such as a visualization of the surgical path.
- The applications for this live surgical aid are widespread, from the intended use of intraoperative aid to medical training, preoperative planning, and assisting to other surgical operations.

In conclusion, NeuroLens has the potential to **revolutionize brain surgery** and **significantly improve surgical outcomes for millions of patients.**