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W. Aigner, D. Archambault, and R. Bujack
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Safe to remove? Exploring the use of registration uncertainty for improving decision-making during tumor resection surgery

Mahsa Geshvadi[1,2,3], Reuben Dorent[2,3], Colin Galvin [2,3], Nazim Haouchine[2,3], Tina Kapur[2,3], Steve Pieper[2,3,4], Mark Vangel[2,3], William M. Wells[2,3], Alexandra J. Golby[2,3], Daniel Haehn[1], Sarah Frisken[2,3]

[1] University of Massachusetts Boston [2] Brigham and Women's Hospital
[3] Harvard Medical School [4] Isomics, Inc.

Figure 1: *Exploring various methods for visualizing image registration uncertainty during image-guided neurosurgery with our software.*

Abstract

Neurosurgeons need to precisely localize and resect tumors without damaging critical brain tissue. However, deformation of the brain (i.e., 'brain shift') and other factors introduce uncertainty during image-guided surgery. Together with neurosurgeons, we study ways to communicate this uncertainty while minimizing cognitive load in the complex surgical environment. We performed a requirements analysis, including semi-structured interviews and prototype evaluations, and learned that optimal uncertainty communication is surgeon- and situation-specific. We present UVisExplore, a visualization software that allows qualitative and quantitative exploration of the effectiveness of a broad range of methods for communicating uncertainty. Additionally, we simulate the cognitive decision-making process during tumor resection through a game to evaluate different uncertainty visualization techniques. Beyond its primary application, UVisExplore has the potential to catalyze substantial advancement. It can address the complexities of uncertainty visualization in various applications by enabling users to explore and combine different visualization techniques. Our software is publicly available.

CCS Concepts
• ***Human-centered computing*** → ***Visualization toolkits;***

1. Introduction

A fundamental objective of brain tumor surgery is to maximize the extent of brain tumor resection while minimizing damage to surrounding brain tissue, ultimately increasing patients' overall survival [SPM*11, GD19]. In other types of cancer surgery, a wide margin around the tumor (i.e., a safe margin) can be resected to ensure complete resection of the tumor. However, in brain surgery, aggressive resection could damage critical nearby brain structures, leading to neurologic deficits.

To maximize outcomes, neuronavigation has helped considerably in providing intraoperative guidance to surgeons, allowing them to visualize the position of their surgical instruments relative to the tumor and critical brain structures visible in preoperative imaging [MPHH*15]. However, neuronavigation requires precise alignment (registration) between the patient's head and the preoperative imaging, which is typically off by several millimeters at the start of surgery [FLJ*19]. Moreover, the validity of the preoperative image progressively decreases due to brain shift as the surgery progresses, making accurate intraoperative guidance more critical for achieving maximally safe tumor resection.

Brain Shift. Brain shift is the dynamic and non-rigid deformation of the brain caused by various physical, surgical, and biological phenomena, such as osmotic concentration, fluid levels, head position, and tissue resection (Figure 2). Brain shift invalidates the initial registration between the patient's head and preoperative imaging and violates the rigid body assumption of most commercial neuronavigation systems [GKOH*21].

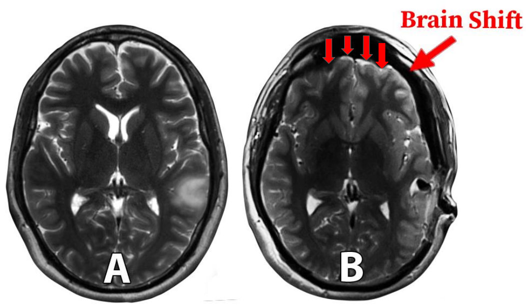

Figure 2: *An illustration of brain shift: (A) Preoperative MRI, (B) Intraoperative MRI*

Compensating for Brain Shift. Brain shift can be estimated by registering preoperative imaging (typically Magnetic Resonance Imaging (MRI)) with intra-operative MRI [NGC*00], surgical cameras [HJI*20] or ultrasound [XRC*19]. Intraoperative MRI provides anatomical details that neurosurgeons can easily interpret, but acquiring an intraoperative MRI typically can require, on average, 90 minutes of additional operating room (OR) time and is expensive and disruptive to surgery [ASM*23]. Also, most hospitals do not have access to intraoperative MRI. Surgical cameras can also be used to compensate for brain shift by registering preoperative MRI on images of the brain surface acquired intraoperatively using the surgical microscope [HJI*20]. These techniques have the advantage of flexibility, but need the brain surface to be visible constantly and are of limited use during the resection stage. Intraoperative ultrasound imaging is an inexpensive and real-time alternative to previous imaging techniques that can be used continuously during surgery (pre-dural and post-dural opening and during resection). However, visually estimating the brain shift using ultrasound images is challenging because ultrasound images are difficult to interpret and may not show tumor margins clearly [DHK*23, DTH*24], and although image registration methods between preoperative MRI and intra-operative ultrasound exists [XRC*19], they are prone to errors that vary spatially, leading to spatially varying uncertainty.

Visualizing Registration Uncertainty. Registration uncertainty can reduce the surgeon's confidence in neuronavigation. When available, we hypothesize that providing a visualization of the spatial distribution of registration uncertainty will help surgeons know where they can and cannot trust navigation. However, effectively conveying the spatial distribution of registration uncertainty remains a significant challenge. Some studies have attempted to provide general methods for visualizing uncertainty [Wei22] [GSWS21]. However, our initial investigations through informal interviews found that surgeons find many uncertainty visualization methods overwhelming, particularly in complex surgical environments where cognitive load is high.

We study the gap between existing uncertainty visualization techniques and the practical integration of uncertainty visualization into surgical procedures. The complexity of the surgical environment and diverse personal preferences among surgeons require tools for exploring, adapting, and evaluating uncertainty visualization methods. We developed UVisExplore, a visualization application that integrates various uncertainty visualization techniques into a software module in 3D Slicer [FBKC*12]. In addition to existing methods, we also incorporated the following novel methods for visualizing and communicating uncertainty:

- **Surgeon-centric**: This method introduces four visualization modes that focus on uncertainty visualization at the tip of the surgical instrument.
  These modes include:
  1. A mode in which the user is alerted with sound when the instrument tip enters or exits a region where the uncertainty is above a specified threshold (e.g., 3 mm).
  2. A mode in which the visualization flickers when the instrument tip enters or exits a region where the uncertainty is above a specified threshold (e.g., 3 mm).
  3. A mode that displays the uncertainty at the instrument tip using a text overlay.
  4. A mode in which the uncertainty is visualized with a color map only around the instrument tip.

  The modes include providing warnings based on specific thresholds, meaning that if the uncertainty exceeds a certain level, the user is alerted. This mode uses a binarization method for communication. Another mode displays the numerical values of uncertainty in millimeters and adjusts the size of the cursor based on the uncertainty value as the user moves the cursor.
- **Tumor-based**: This method draws minimum and maximum offset volumes to focus on uncertainty at the tumor boundary. These two offsets create a space within which the ground truth is expected to lie.

More details on these techniques can be found in the Uncertainty Visualization Methods section.

Additionally, we developed a game in 3D Slicer to evaluate different uncertainty visualization methods and assess their usefulness. This game acts as a proxy for the decision-making process under uncertainty during tumor resection surgery. It has proven to be a valuable tool for introducing the concept of registration uncertainty to surgeons and for observing and evaluating user preferences within a set of controlled environments and tasks.

Contibutions:

1. **Innovative methods for visualizing uncertainty:** We introduce two new methods tailored for brain tumor resection: surgeon-centric and tumor-based uncertainty visualization.
2. **A system for exploring uncertainty visualization methods:** We present UVisExplore, a software system for exploring and

evaluating different uncertainty visualization methods. The paper provides detailed explanations for the significance of each chosen method.

3. **A new game-based approach for quantifying the effectiveness of uncertainty visualization techniques:** We developed a game that simulates the decision-making process under uncertainty during tumor resection. We use our game to observe how users customize uncertainty visualization and to measure the impact of uncertainty visualization on outcomes.

2. Related Work

Uncertainty has been studied in various domains since the 19th century [PWL96]. Considering uncertainty requires two essential components: 1) quantifying uncertainty; and 2) conveying the quantified values to the observer. There has been growing interest in both of these research areas during the past few decades. This work focuses on effective uncertainty visualization, specifically how to visualize image registration uncertainty during image-guided tumor resection surgery. Our work builds on the important contributions of many others, as outlined below.

Uncertainty Visualization Studies have been done to provide an overview of existing methods for visualizing or communicating uncertainty, offering different perspectives on uncertainty visualization. Weiskopf et al. [Wei22] presents a general overview of uncertainty visualization techniques and some examples of applying these techniques in bioinformatics. They focus on exploring layouts for advanced uncertainty visualization. Gillmann et al. [GSWS21] provides an overview of uncertainty in medical imaging. Their paper explores three sources of uncertainty: image acquisition, transformation, and visualization. It focuses mainly on using colors to convey uncertainty and introduces available visualization techniques for various imaging modalities, including magnetic resonance imaging (MRI) and ultrasound. Similarly, Pang et al. [PWL96] propose a classification system for uncertainty visualization techniques with five characteristics: value, location, data extent, visualization extent, and axes mapping. Ristowsky et al. [RPHL14] introduces a taxonomy for uncertainty in medical imaging. They categorize different types of uncertainty based on their factors, like spatial locations where the uncertainty is discrete or continuous, 2D or 3D, etc. Padilla et al. [PKH20] provide a variety of application-specific approaches. They conclude that uncertainty visualization has no one-size-fits-all solution and emphasize considering design choices. The paper highlights the complexity of uncertainty visualization and the importance of empirical testing to ensure the effectiveness of visualizations. These studies guided our understanding of factors to consider in visualizing uncertainty and underscored the complexity of uncertainty visualization.

Brodlie et al. [BAL12] categorized uncertainty visualization algorithms into three distinct classes: dense, sparse, and embedded. Dense visualizations display data at every point within a domain, whereas sparse visualizations focus on extracting and highlighting significant features, such as contour lines. The embedded approach involves placing visualizations into a higher-dimensional display space. For dense visualizations, they introduced two distinct approaches to visualizing uncertainty in contouring: value uncertainty and positional uncertainty. Value uncertainty visualizes the uncertainty along the mean contour line, often using techniques like uncertainty ribbons, where the contour line's thickness or color indicates the uncertainty level. Positional uncertainty visualizes the range of possible contour lines for a given threshold, illustrating the variability in the independent variable space, commonly visualized with methods like spaghetti plots.

Several prior approaches for providing uncertainty visualization use glyphs [BHJ*14, JS03, PWL96] and color overlays [BDH*15, GSWS21]. Less conventional approaches include the use of Augmented Reality [SHB*11] and animation [DKLP02, LLPY07, ESG97]. Grigoryan and Rheingans proposed a method for visualizing the probabilistic uncertainty of the shape of a 3D surface model [GR02]. Osorio and Brodlie developed methods to visualize uncertainty during contouring [OB08]. In other contexts Kay et al. [KKHM16] integrated interactive control in a system to help users understand uncertainty in predicting bus arrival times. Greisi et al. [GJS*18] also implemented an application that gave users some control over uncertainty visualization, albeit in sensor measurement and for visualization of discrepant information. Simpson et al. [SMC*06] performed a study on osteoid osteoma excision surgical task. The authors used volume rendering to visualize the uncertainty, which allows viewing the path distribution as a 3D volume or 2D cross section. The authors conducted a user study to evaluate the effectiveness of the visualization method. The task mimicked the excision of a deep bone tumor. The results showed that the visualization method resulted in a statistically significant reduction in the number of attempts required to localize a target.

For volumetric data uncertainty visualization studies, Athawale et al. [AMS*21] present a nonparametric statistical framework for visualizing uncertainty in volumetric data using direct volume rendering (DVR). They employ quantile interpolation to integrate nonparametric probability density functions (PDFs), thus enhancing the precision of uncertainty visualizations. Their approach includes extending to 2D transfer functions (TFs) for better classification and utilizing a quartile view to highlight reconstruction variability across different data quantiles. This method demonstrates improved accuracy over traditional parametric models. Djurcilov et al. [DKLP02] use two approaches to visualize uncertainty in volumetric data. Their inline DVR method incorporates uncertainty directly into the rendering process using transfer functions, mapping data to color and uncertainty to opacity. Their post-processing techniques modify volume-rendered images to indicate uncertainty by adding speckles, depth-shaded holes, noise, or textures. We explored a similar approach, which adds Gaussian blurring or noise that is correlated with uncertainty. Liu et al. [LLBP12] proposed Gaussian Mixture Model-based volume visualization, which uses per-voxel Gaussian mixture models to represent and render volumetric data with uncertainty. This method reduces data storage and utilizes the GPU to provide real-time rendering. It visualizes uncertainty through animated flickering and detailed still frames. However, its visual complexity makes it unsuitable for the operating room. Potter et al. [PGA13] use entropy as a summary statistic for categorizing data, such as each voxel of brain tissue, into one of 11 types and visualize uncertainty by highlighting high-entropy regions in white. This method highlights regions where the assignment to a particular category is uncertain, as indicated by higher entropy values. However, this approach changes the data representation and can result in the loss of important information, making it unsuitable for our context.

For neurosurgery, Frisken et al. [FLH*22] proposed a method that composes uncertainty contributed by image segmentation and brain shift into a single risk volume and conveys this risk to the surgeon during surgical planning using soft boundaries and volume rendering. That paper focuses on modeling and visualizing uncertainty during path planning, while our focus is on developing visualization methods that are effective in the complex environment of the OR. Similarly, Diepenbrock et al. [DPL*11] proposed a method to give neurosurgeons a quick overview of the most important structures at risk during surgical planning. Their methods employed an intuitive red-blue color mapping in which nearby at-risk critical structures are rendered red. They introduce a workflow for path planning and target the planning phase. However, their approach does not account for registration uncertainty, which is the central aim of our study.

Our motivation for this study was to explore a wide variety of existing and novel uncertainty visualization techniques in order to find the most effective method. It quickly became clear that there was a need for a software tool that would allow users, particularly neurosurgeons, to explore visualization techniques where we could sandbox new ideas and develop and test ways to compare and evaluate uncertainty visualization methods.

3. Iterative Design Process

We began our iterative design process by implementing multiple uncertainty visualization methods prototypes while obtaining feedback from neurosurgeons and image-guided neurosurgery researchers through informal interviews. Our prototypes included traditional uncertainty visualization methods, such as color overlays, and innovative approaches, such as our “surgeon-centric” methods. These methods are detailed below. Throughout interviews and demonstrations, we showcased visualizations, inviting participants to express their ideas and insights regarding their perceived effectiveness. We used the think-aloud protocol [Jää10]. This provided us with user insights, feedback, new ideas, and some guidance into what worked well and what did not. During this stage of the design process, users expressed a strong desire for the ability to control visualization parameters so they could interactively explore different possibilities and variations.

To address this desire, we developed UVisExplore with an intuitive user interface to allow users to explore a variety of uncertainty visualization methods and method features. A critical part of the design process was carefully selecting variable features for each method. We selected these features based on ideas gathered from interviews and features used in existing uncertainty visualization methods.

The key steps in our iterative design process can be summarized as follows:

1. **Requirement Analysis:** In this step, we engaged with domain experts to gain insights into uncertainty in their field and asked questions like "What does uncertainty mean in this context? When do you use it?" This step helped us define our project’s scope and identify our solution’s key requirements.
2. **Prototype Implementation:** After thoroughly understanding the problem and its requirements, we created initial prototypes for color overlay and our surgeon-centric techniques.
3. **User Feedback Gathering:** Through interviews, we collected valuable feedback to refine and enhance our prototypes.
4. **Application Development:** Responding to user preferences, we developed UVisExplore to facilitate dynamic real-time exploration of uncertainty visualization methods.
5. **Refinement Through Feedback:** We iteratively refined the features of UVisExplore based on user feedback, enhancing existing features and incorporating new ones as necessary.

Our iterative design process shares similarities with the Design Study Methodology proposed by Sedlmair et al. [SMM12]. Both approaches emphasize close collaboration with domain experts, iterative prototyping, and continuous refinement based on feedback. Like the Design Study Methodology, our process involved extensive requirement analysis, where we engaged with neurosurgeons and image-guided neurosurgery researchers to understand their needs and challenges. We followed an iterative cycle of prototype development, user feedback gathering, and refinement to ensure that our visualization methods effectively addressed the specific demands of the surgical environment.

3.1. Requirements Analysis

In medical applications, it has been shown that keeping the cognitive load minimal is a critical requirement for uncertainty-aware visualization [GSWS21]. Thus, this was a fundamental requirement throughout our entire design process. It was essential to understand the unique environment and the surgeon’s needs during tumor resection so we could develop effective uncertainty visualization methods. To establish our design principles and requirements, we conducted semi-structured interviews with neurosurgeons and image-guided neurosurgery researchers. We also observed multiple tumor resection surgeries to understand the challenges they face in real surgical scenarios.

Based on the insights gained from our interview sessions, we identified the following general design requirements:
R1. Give users control over the way uncertainty is visualized: Different surgeons have different styles and preferences, and different situations have different needs and background cognitive loads. Empowering users to explore different uncertainty visualization methods and method features allows them to choose options that align with their needs before taking them to the operating room. Additionally, it helps users communicate their responses, feedback, and ideas for improvements to technical researchers as they explore the available methods in real time.
R2. Make it easy to switch between different methods and method features: Tumor resection surgery moves through multiple stages, including planning, preparation, tumor resection, and assessment (and not always in a linear fashion). Surgeons may have different needs depending on the current stage, and the role of uncertainty visualization may vary from stage to stage. Thus, surgeons may want to switch between different uncertainty visualization methods to adapt to current conditions. In a research environment, this task can be done by technical assistants, but for translation to clinical practice, it should be easy to switch between

methods to ensure a smooth workflow.

R3. Communicate numerical values: Surgeons need to understand uncertainty both implicitly and explicitly. In interviews, surgeons mentioned that in some situations, they need a quick indication of whether or not it is safe to resect a specific spot. In these cases, a graphical representation of uncertainty values suffices. However, in certain critical situations, they need to know exact uncertainty values (e.g., a millimeter measurement) to make precise decisions.

3.2. Data and Uncertainty Quantification

For this study, we utilize pre-operative images of brain tumors from the ReMIND dataset [JDK*24]. Specifically, we select post-contrast T1 scans along with their manual delineations of the tumors. From this dataset, 2D axial slices showing brain tumors were selected from two patients to be used in the proposed game. While these images were aligned to the patients' heads using a navigation system, registration errors are anticipated during surgery due to brain shift, especially near the tumor. However, we do not have access to these actual registration errors.

To address this, we simulate the registration errors and the associated registration uncertainty quantification. This approach allows us to create a controlled environment for validating the visualization of uncertainty in image registration. The game presents users with a registered pre-operative image and its corresponding uncertainty measurements, indicating confidence in the registration results for each pixel in millimeters. To ensure that the uncertainty measurements serve as an upper bound for the registration error, we simulate them together.

We begin by simulating the uncertainty map as an upper bound of the true displacement field using Perlin noise [Per02] for each 2D dimension. Perlin noise, known for its structured and locally smooth characteristics, has previously been used to simulate resection cavities [PGDR*21]. To mimic realistic conditions where brain shift does not affect the skull, the displacement field is set to zero outside the brain. Given that most deformations are expected to occur around the tumor, we multiply the Perlin noise by a Gaussian dilution of the binary segmentation mask of the tumor. This approach leads to higher noise in areas with expected higher deformation.

Next, we scale the Perlin noise to define maximal displacements in millimeters to 4mm. This rescaled Perlin noise is considered an upper bound of the displacement field associated with the residual registration errors. The uncertainty map is then generated by calculating the Euclidean distance of this upper bound in millimeters. We then create the true but hidden registration error by multiplying the upper bound of the displacement field by another Perlin noise normalized between 0 and 1. This ensures that the registration error is always upper-bounded by the uncertainty.

Finally, we create a triplet comprising a registered image where brain shift is not perfectly corrected, an uncertainty map indicating the upper bound of the registration error, and the actual registration errors as ground truth. This triplet provides a comprehensive dataset for users to analyze, offering insights into the areas of the image that are trustworthy and the extent of potential misregistrations. It also creates a controlled environment to validate uncertainty visualization techniques, ensuring that the uncertainty measurements are well-calibrated.

3.3. UVisExplore Software Overview

Our software is designed as a custom Python module in 3D Slicer [FBKC*12], an open-source medical image visualization platform. The user interface is divided into four main sections; each can be expanded or contracted independently, facilitating easy switching between uncertainty visualization methods (Satisfying R2). The interface uses sliders and checkboxes for selecting and adjusting method features and for real-time visualization of changes. Figure 3 shows a screenshot of the interface.

4. Uncertainty Visualization Methods

This section presents the uncertainty visualization methods we have implemented in our software and the features we selected for interactive modification. We also clarify their utility and discuss the design process that led to their development. The user interface for our software has four primary sections, as outlined below.

4.1. Color Overlay

In this method, a color map encoding uncertainty is overlaid on top of the underlying data (in this case, a 2D slice of a 3D image).

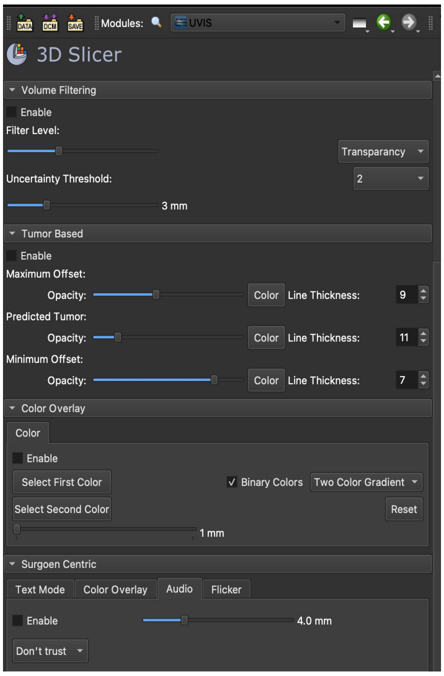

Figure 3: *Overview of UVisExplore in 3D Slicer for exploring uncertainty visualization methods.*

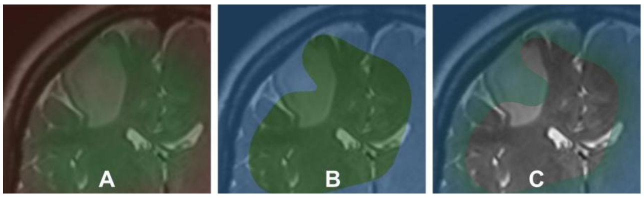

Figure 4: *Color Overlay variations: (A) Customizable color overlay for visualizing registration uncertainty. (Here, red indicates high registration uncertainty, green low). (B) A binary visualization option enables users to categorize uncertainty based on a user-selected threshold (e.g., above or below 3 mm of registration uncertainty). (C) The color overlay can be set to be visible only when the uncertainty is above the user-selected threshold.*

In Figure 4A, red indicates areas with the highest registration uncertainty, while green indicates areas with the lowest uncertainty. Intermediate uncertainty values are represented as a gradient between these two colors. In prototype evaluation, we presented this method to surgeons and allowed them to scroll through the 3D volume. Based on feedback from multiple surgeons during interviews, it became apparent that 1) color choice is a feature that needs to be customizable due to a large range of personal preferences, and 2) overlay opacity needed to be customizable so surgeons can adjust the visualization depending on surgical context (e.g., for preoperative planning, for use in bright and dark environments, or to avoid obscuring other important information in the image such as segmented structures). Based on insights from interviews, we added the ability to visualize uncertainty in a binary form as shown in Figure 4B. This method allows surgeons to set a threshold, such as 3 millimeters, below which they might feel safe ignoring registration uncertainty. As a slight modification of this method, surgeons can remove color coding in areas where uncertainty is less than a specified threshold (Figure 4C) to further reduce visualization complexity.

Limitations: While color overlays have been commonly used for visualizing uncertainty, we found that surgeons and other clinicians found that they obscured the underlying image, making it difficult to see important details.

4.2. Tumor-Based Visualization

In tumor resection, registration uncertainty is most critical at the tumor boundary because this is where the surgeon must determine whether it is safe to remove. We developed novel methods that focus on uncertainty visualization at the boundary of the segmented tumor.We use offset surfaces to represent the uncertainty of the boundary, in contrast to the work of Grigoryan et al. [GR02], which encodes uncertainty on the surface using color maps.Our method visualizes both minimum and maximum offsets, providing a safe zone inside the minimum offset where surgeons can operate more confidently and faster. This visualization is represented by a simple line, avoiding the complexity of color coding. Using the segmented boundary and the uncertainty volume, we compute the uncertainty, x, at each point on the boundary, indicating that the tumor could be within ±x millimeters of that point.

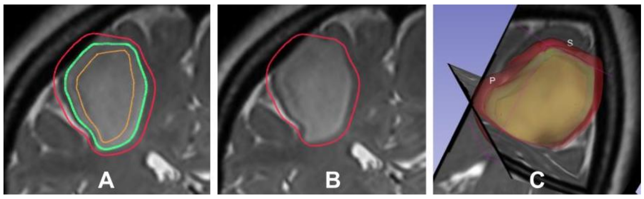

Figure 5: *Tumor-based variations: (A) The boundary of a segmented tumor (green) with offset boundaries in positive (red) and negative (yellow) directions given local registration uncertainty at the segmented boundary. (B) The boundary (red) represents the maximum extent of segmented tumors according to the local uncertainty value. (C) A 3D view displaying all three volumes provides a spatial visualization of the potential tumor volume.*

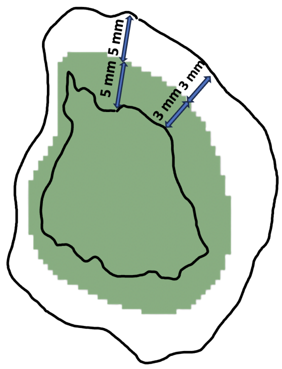

Figure 6: *We generate 3D models of minimum and maximum tumor boundaries by offsetting each point along the tumor's segmented boundary. This offset is determined by the local uncertainty value at each point (e.g., 3mm or 5mm) and is applied in a direction perpendicular to the boundary.*

There are multiple methods for computing offset surfaces. In our software, we first computed a surface from the segmented tumor volume using 3D Slicer's Grey Scale Model Maker module. Then, for each point in the model, we offset the point in the positive and negative direction of the surface normal to create points in the maximum offset surface and minimum offset surface, respectively (see Figure 6). In our software, these two offset surfaces can be visualized in 2D as contour overlays and in 3D as surfaces (Figure 5). This visualization method helps surgeons recognize that the actual tumor boundary lies within the offset surfaces. Based on feedback from surgeons, we introduced a feature to our tumor-based uncertainty visualization method that allows surgeons to adjust the transparency of the offset volumes or remove them entirely (Figure 5B). Other feedback included a desire to incorporate "additional certainty/uncertainty for key adjacent structures (e.g., brain vessels) inside the lowest uncertainty cut-off.

Limitations: While this method effectively visualizes uncertainty at tumor boundaries, it lacks visualization for other image regions.

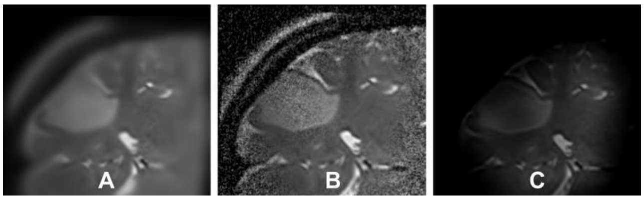

Figure 7: *Image filtering methods: (A) Blur Filter: The image is blurred using a local Gaussian filter based on the local uncertainty value. The image is not blurred where the uncertainty is below a minimum threshold. (B) Noise Filter: Introduces white noise to the image to represent uncertainty. Higher noise levels are used where uncertainty is higher. (C) Transparency Filter: Image transparency is locally adjusted based on local uncertainty.*

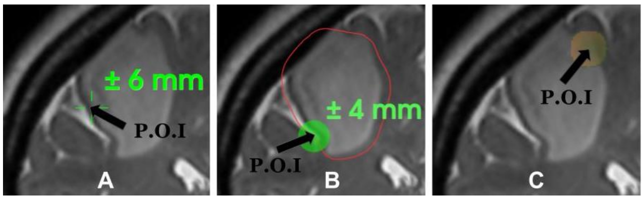

Figure 8: *Surgeon-centric methods visualize uncertainty near the surgeon's tracked instrument. The uncertainty at the instrument's location is visualized through A) displaying the uncertainty in millimeters at the point of interest, B) a resizable cursor that alters size based on local uncertainty or C) the color overlay technique, which is visualized only around the surgeon's instrument.*

4.3. Uncertainty-Based Image Filtering

Inspired by the work of Djurcilov et al. [DKLP02], this feature provides an alternative to color overlays for representing uncertainty. The MRI image is locally filtered according to local uncertainty values. For example, the image may be blurred or have noise added to it in regions of high uncertainty (Figure 7). Surgeons can choose uncertainty thresholds that control the amount of filtering applied to different image regions. Setting a minimum threshold, below which the image is not filtered, allows them to leave regions of low uncertainty unaffected.

Limitations: This method intuitively represents uncertainty by altering uncertain regions, yet it poses challenges by obscuring details in highly uncertain areas.

4.4. Surgeon-Centric Methods

We introduce a surgeon-centric uncertainty visualization approach, similar to the sensitivity lens in Lundström et al.'s work [LLPY07]. In this approach, uncertainty visualization is focused where the user's interest is focused, specifically at the location of their tracked surgical instrument (Figure 8). The innovation of this approach is its four different modes, all centered on the surgical probe and specifically designed for tumor resection surgery.

A. Text. At critical time points during surgery, surgeons may need to know the estimated uncertainty value at specific locations. Based on initial feedback, we added a method that displays local uncertainty as a text value (Figure 8A) and encodes it in the cursor size (Figure 8B). Users can turn the text representation on and off and specify the cursor type. For example, if a spherical cursor is chosen, the cursor radius reflects the uncertainty value in millimeters.

B. Color overlay. In surgeon-centric color overlays, we limit color overlay visualization (whose features are set in the Color Overlay section of our software's user interface, described above) to a sphere surrounding the tracked instrument. (Figure 8C)

C. Audio. An alternative approach for surgeon-centric visualization is to warn when the surgeon's instrument moves into a region with high uncertainty. This is similar in concept to the binary alternatives described above for color overlays and image filtering. Here, the surgeon specifies an uncertainty threshold, below which they consider the image registration to be 'safe' (because the uncertainty is low) and above which they consider the registration to be 'unsafe' (because the uncertainty is high). Audio communication of uncertainty can provide a beneficial alternative to visual communication, which many people may interpret as abstract [GJS*18]. Thus, we implemented an audio-based method to indicate when the surgeon's instrument moves into regions of high uncertainty [LWS96]. Various audio warning signals can be specified (two beep signals and the phrases "trust/don't trust").

D. Image flicker. Using ideas inherent to our audio-based communication, we implemented a warning method that causes the image to flicker when the surgeon's instrument moves out of the 'safe' region. Like the audio method, this method is designed to grab the surgeons' attention quickly.

These features can be combined. Additionally, the audio and image flicker modes provide a binarization for uncertainty communication, notifying the surgeon only if the uncertainty exceeds a specific threshold.

Limitations: Surgeon-centric methods focus on visualizing uncertainty around their tracked surgical instruments. This approach minimizes distractions from other image areas, simplifies the visualization, and enables the surgeon to concentrate on the area of interest. However, the primary limitation is the inability to provide a comprehensive overview of the entire image.

4.5. Formative evaluation

As part of our iterative feedback process, we presented UVisExplore to 15 subjects, including neurosurgeons, medical fellows, and image-guided neurosurgery researchers. Given UVisExplore's diverse range of visualizations, our objective in this evaluation phase was to get feedback and suggestions.

Participants: One neurosurgeon, one medical doctor (M.D), three senior image-guided neurosurgery researchers, and ten junior researchers with computational and/or pre-medical backgrounds.

5. Evaluation

First, we explained the concept of registration uncertainty to ensure all subjects understood the goal of uncertainty visualization.

Table 1: *Participant Preferences for Uncertainty Visualization*

Participant #	Preferred Mode
1	Tumor + Audio
2	Transparency Filter
3	Surgeon-centric + Tumor
4	Text + Tumor + Surgeon
5	Depends on Situation
6	Tumor + Audio/Text
7	Noise + Transparency Filter
8	Text
9	Tumor + Audio
10	Tumor
11	Transparency + Noise + Text
12	Transparency + Noise + Text
13	Transparency Filter
14	Tumor
15	Noise + Text + Transparency + Tumor + Audio

We presented our uncertainty communication software and demonstrated the visualization methods and method features we refined through our iterative design process. We asked subjects to fill out an online survey during the presentation. Questions in the survey were designed to learn subjects' impressions of the intuitive and useful visualization methods and their features and gather suggestions for refining the features. After each method was presented, we asked subjects to rank the methods on our survey scale from 1 to 5 (5 being highly intuitive and 1 being the least intuitive). Finally, we asked subjects to specify their favorite combination of methods and compared responses. Information about each subject's degree type (e.g., MD vs. PhD) and experience level (e.g., research trainee vs. senior researcher/clinician) was collected in the survey. Tumor-based visualization was considered to be the most intuitive. 53% of subjects specified tumor-based methods, and 66% specified a combination of different methods. The neurosurgeon specified that the most helpful visualization method depends on the situation and emphasized the need for a customizable tool. In an open question at the end of the survey, many subjects made valuable suggestions, which we have used to improve our uncertainty visualization software. Table 1 shows the participant's preferred visualization method.

The feedback gathered through this evaluation helped us refine our uncertainty visualization software. However, it is important to note that evaluating intuitiveness based on a presentation alone may not fully capture the effectiveness of the visualizations in practical settings. Thus, a more comprehensive evaluation approach is necessary, as discussed in the following section.

5.1. A Game for Evaluating the Effectiveness of Different Uncertainty Visualization Methods

Because uncertainty is intuitively communicated and is inherently related to probabilities, it is challenging to evaluate the effectiveness of uncertainty visualization. It is also important that the effectiveness be evaluated under realistic conditions [HQC*19]. However, we needed to perform more evaluation before moving to the operating room for the following reasons:

- Our access to observation in the operating room is relatively rare (1-2 per week). This reduces our ability to collect sufficient data and iterate efficiently.
- In the operating room, the main focus is necessarily on the patient. If a visualization method is cumbersome or not intuitive, surgeons do not have the time or patience to consider alternative methods or features. Thus, iterative refinement in the operating room is impractical.
- The number of surgeons available for testing uncertainty visualization methods is relatively small. Thus, it is important that we narrow the choice of visualization methods as much as possible before evaluating them in the operating room. For this reason, we seek a more controlled, simulated environment for evaluating methods.
- We require a simulation environment for evaluating the effectiveness of various visualization methods because it allows for exploring outcomes without real-world consequences. In a simulated setting designed as a game, users can afford to make mistakes, such as mistakenly resecting healthy tissue, which in a real operation could have significant implications for patient health. This approach enables users to experiment with different decisions informed by the visualization tools, facilitating a deeper understanding of their utility and limitations without risking patient safety.

For these reasons, we developed a game that simulates the decision-making process required for tumor resection. This decision-making process includes the situation where subjects must decide whether to resect a specific area. The game has been integrated into our visualization tool, allowing users to explore different techniques and assess how different uncertainty visualizations guide their decision-making. By implementing a scoring system, we encouraged participants to experiment with various uncertainty visualization methods, select the most effective ones, and try to achieve the highest score. Detailed instructions for the game are provided in the Game Design section. Sessions lasted approximately 15 minutes.

Game Design:

We developed a game inspired by the process of tumor resection surgery to assess the effectiveness of our uncertainty visualization tool quantitatively. The game presents users with a misregistered image with corresponding uncertainty registration measurements, indicating an upper bound of the registration error for each pixel. The goal is to identify the location of the well-registered tumor, given the misregistered image and this uncertainty measurement. This uncertainty is visualized to help participants make informed decisions about tumor resection. They can customize and try different uncertainty visualization techniques.

As mentioned in Section 3.2, the ground truth segmentation mask has been obtained by deforming the segmentation mask of the misregistered image, allowing us to know exactly where the well-registered tumor is. To ensure that the provided uncertainty is trustworthy, the registration error is lower than the provided uncertainty measurements. An example case is shown in Figure 9.

The user task is to carve out where they think the tumor is, considering the predicted boundary and the registration uncertainty.

They do this twice, first without being able to visualize the uncertainty and then with the uncertainty visualization tool. Our goal is to see if uncertainty visualization helps them more effectively identify true tumor regions (our ground truth) and if uncertainty visualization improves their scores or not. The scoring system is designed so that going outside the true tumor boundary results in negative points, while resecting the tumor inside the true boundary earns positive points. (Figure 10 and 11).

Participants are also ranked on a leaderboard based on their positive and negative scores. The ranking system calculates the score for ranking as:

$$\text{ranking score} = \text{positive score} - 2 \times \text{negative score} \tag{1}$$

emphasizing the greater impact of incorrect resections.

When ready, participants use the mouse to start carving out tumors in the MRI image. Scores and the extent of resection are recorded to facilitate a quantitative evaluation of the tool's effectiveness. Participants are encouraged to explore different visualization techniques to identify the one that most effectively conveys the uncertainty present in the deformed image.

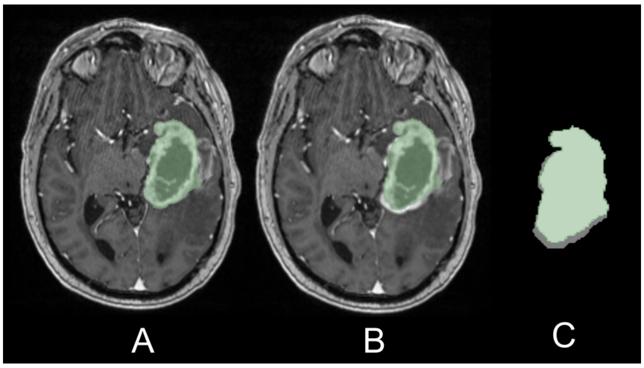

Figure 9: *Brain Image Deformation: A displays the image as viewed by the participants, while B presents the ground truth, which is slightly shifted. C highlights the difference between the two boundaries: the ground truth and the participant's view.*

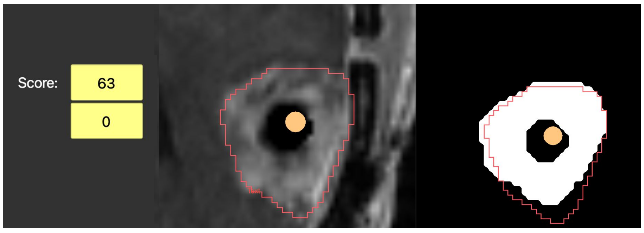

Figure 10: *The player has started the game and is carving out the tumor, staying within the ground truth boundaries and receiving scores.*

Game Instructions:

We started this evaluation with a 5-minute tutorial. Players are informed that the image they see is after the brain shift has happened, and it has been deformed.We explain the uncertainty visualization techniques to them in a random order to prevent bias.

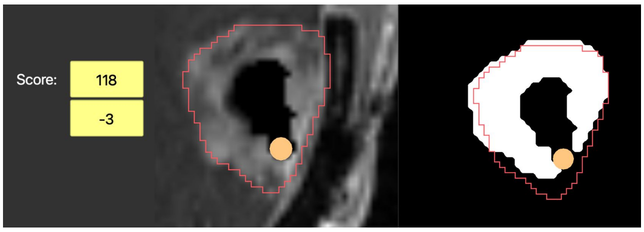

Figure 11: *The player has moved outside the ground truth boundaries, resulting in negative scores.*

The game consists of two levels. Each level uses a different tumor image:

1. **Training level.** The first level ensures that the players understand the game, the goal, and the concept of uncertainty correctly. At this level, players can see the ground truth while playing. They can also see their negative and positive scores to understand the effects of their decisions. When the game starts, players should hover their mouse over the area they want to resect. As they move the mouse, they will resect the tumor. They will gain positive points if they stay within the ground truth boundaries. If they go outside the ground truth boundary, they will lose points.
   Players start the game with a specific visualization. They can modify the visualization and explore different techniques. They can also reset the game to play it with other visualization techniques. The time for this level is limited to provide equal practice opportunities for all participants. By the end of the training level, they had chosen the method they would use for the challenge level, and they could not modify it at the challenge level.
2. **Challenge level.** In the second level, players do not have access to the ground truth or their scores, simulating a real scenario where no feedback is provided. Additionally, there is no undo option, and players have only one chance to perform each step.

   Level 2 is performed twice:

   - The first time, players play the game without any visualization, establishing a baseline to see where they would resect without uncertainty visualization, knowing the image is inaccurate.
   - The second time, players perform the same task with visualization. After completing this step, they hit the "Reveal Results" button to see their positive and negative scores with and without visualization. The leaderboard is updated to show their ranking.

   Our hypothesis is that players will achieve higher positive scores and lower negative scores with visualization compared to without it.

Participants: Four Neurosurgeons and one neurosurgery resident

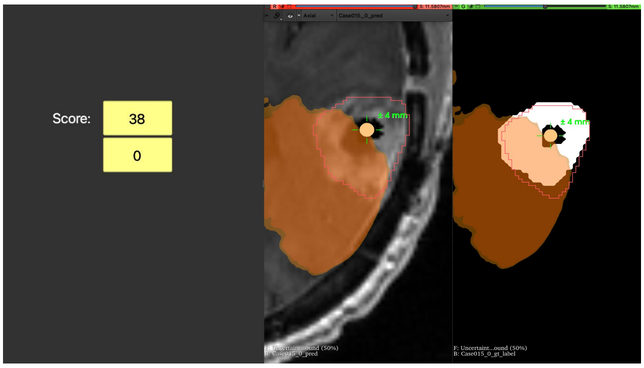

Figure 12: *Screenshot of the first level. The user can view the ground truth and their scores. The ground truth is represented by the white volume. This figure includes an example combination of uncertainty visualization techniques: color overlay and the surgeon centric text mode technique.*

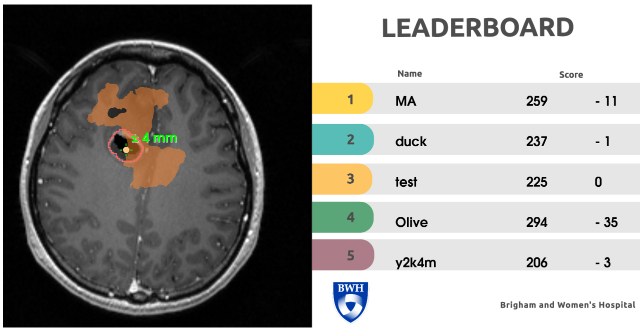

Figure 13: *Screenshot of what user sees in the second. The real game starts where they should play the game without seeing the ground truth and their scores.*

(PGY-5), one Medical Doctor (M.D) without neurosurgery training, and three computer scientists

Results:

Participants played the training level first and then the challenge level. We observed their questions and feedback during both levels and logged their visualization selections and their scores. Table 1 shows the visualization method they chose for the Challenge level.

The results show that after the training level, 88% of participants included the tumor-based technique in their choices, and 88% included the text mode. 77% explored multiple techniques during the training level and chose their method based on their exploration.

None of the participants chose the filtering, flicker, or audio modes. Players stated that they found it difficult to set a useful threshold for these modes.

All the neurosurgeon participants selected the tumor-based visualization with text mode, and one of them also used the color overlay. Therefore, the text mode and tumor-based were included in all selections satisfied R3 of the requirements above in Section 3.1 that quantitative values of uncertainty be provided.

Table 2: *Level 2 Game Scores Before and After Visualizing Uncertainty. Participants 1-3 are computer scientists, Participant 4 is an MD without neurosurgery training, Participants 5-8 are neurosurgeons, and Participant 9 is a neurosurgery resident (PGY-5). The best possible score is 404 positive and zero negative.*

Participant #	Without Visualization		With Visualization	
	Positive	Negative	Positive	Negative
1	259	-22	259	-11
2	279	-18	237	-1
3	347	-84	318	-48
4	156	0	169	0
5	163	-24	176	-12
6	315	-33	294	-35
7	262	-26	206	-3
8	284	-23	297	-31
9	264	-6	274	-6

Table 3: *Uncertainty Visualization Selection for each participant. Participants 1-3 are computer scientists, Participant 4 is an MD without neurosurgery training, Participants 5-8 are neurosurgeons, and Participant 9 is a neurosurgery resident (PGY-5).*

Participant #	Selected Uncertainty Visualization Technique
1	Color Overlay + Surgeon Centric Text Mode
2	Color Overlay + Tumor Based
3	Surgeon Centric Text Mode + Tumor Based
4	Surgeon Centric (Color Overlay + Text Mode) + Tumor Based
5	Color Overlay + Surgeon Centric Text Mode + Tumor Based
6	Surgeon Centric Text Mode + Tumor Based
7	Surgeon Centric Text Mode + Tumor Based
8	Surgeon Centric Text Mode + Tumor Based
9	Surgeon Centric Text Mode + Tumor Based

80% of the neurosurgeons found that the color overlay obscured the anatomy. Among these, one neurosurgeon expressed the desire to use the color overlay only before starting the challenge level to get an overview of the uncertainty map and, identify highly uncertain areas, and then turn it off before playing the game. This indicates that different scenarios require different techniques (R1). For example, in a real surgical setting, the color overlay can provide an overview of uncertain areas after registration and uncertainty estimation.

Neurosurgeons are most interested in uncertainty visualization centered on the surgical probe, with the tumor boundary being the most critical area for uncertainty visualization. The selection of tumor-based and text modes by all neurosurgeon participants highlights the effectiveness of our novel techniques. At the end of the survey, we asked neurosurgeons if they would use the selected visualization in the operating room, and 80% responded positively, providing suggestions for improvement.

The challenge level aimed to compare decision-making under uncertainty with and without uncertainty visualization by analyzing both negative and positive scores. All non-neurosurgeon participants received fewer negative scores with uncertainty visualization. One participant didn't get any negative scores at all but achieved more positive scores with visualization. Since negative scores indicate resecting non-tumor areas, which might be healthy brain tissue, reducing negative scores is particularly important. Therefore, we can conclude that the uncertainty visualization is improving decision-making for non-neurosurgeons (Table 2).

The results were more mixed for the neurosurgeons (participants 5-9). We analyzed their performance by plotting their scores on a graph with both negative and positive axes to categorize them into two different behaviors and observe any improvements. However, the results did not support our hypothesis. 60% improved their negative scores and only 40% improved their overall scores with uncertainty visualization.

Post-game interviews provided some insight. Two neurosurgeons explained that they ignored the uncertainty visualization. Without the ground truth image provided at the Challenge level, they relied on their knowledge of anatomy to make decisions. Essentially, they were more conservative near critical structures. Another clinician mistrusted the uncertainty values based on their relation to the surrounding anatomy. This was understandable, given that our uncertainty values were synthesized. This mistrust biased them against the game from the start. Finally, we observed that two of the neurosurgeons spent very little time exploring the visualization options and may not have been fully engaged in the experiment.

6. Discussion and Conclusions

In our study, we developed *UVisExplore*, a software designed to explore, evaluate, and learn about various uncertainty visualization techniques during tumor resection surgery. We believe that integrating uncertainty visualization into clinical practice requires addressing multiple steps, and this tool represents a significant advancement toward that goal. Our study highlighted the need for a tool to explore different visualization methods before selecting the most effective one for real-world applications. We assessed the effectiveness of our tool through a game and tested it with both neurosurgeons and non-neurosurgeons. After exploring different techniques, all neurosurgeons showed a clear preference for tumor-based and surgeon-centric text modes.

We introduced the use of a game paradigm for testing the effectiveness of uncertainty visualization. We developed a game to simulate tumor resection after brain shift to evaluate the effect of uncertainty visualization on surgical decision-making. Using the game, we found that non-surgeons improved their scores when uncertainty visualization was present. Our results were more mixed for neurosurgeons. In general, uncertainty visualization was less helpful to them. However, during post-game interviews, we learned several things that we plan to use to improve our game for future work.

First, we discovered that the simulated tumor deformation must be physically realistic, paying close attention to the direction of brain shift, requiring close collaboration with neurosurgeons. We learned that uncertainty is more significant in critical areas, such as motor function and language regions, where surgeons will make more conservative resections. In the future, we will consider adding a cost function to our scoring system, where critical areas would receive higher negative scores or even result in game over. These insights underscore the importance of considering neuroanatomy when deforming the image and collaborating closely with neurosurgeons to ensure the images are clinically relevant and intuitive. Because our synthetic deformation was not entirely believable (in one case, the brain shifted against gravity), some neurosurgeons mistrusted the visualization and used their prior knowledge instead. In spite of these challenges, we believe that game-based methods are an exciting new direction for evaluating uncertainty visualization.

For future work, we plan to add more levels with a more diverse set of tumor images and implement a cost function for critical brain areas. We aim to make the next version more dynamic, with the brain shifting over the course of the tumor resection. We will also explore different surgical scenarios where visualization is crucial, categorize them, and determine the most effective visualization techniques for each. Additionally, we will enhance the deformation simulation to make them more physically realistic. Furthermore, we plan to use *UVisExplore* as a training tool for neurosurgeons to teach them about uncertainty, improve their understanding of it, and ultimately gain their trust to use it in real surgical settings.

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