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ORIGINAL ARTICLE

Optimizing registration uncertainty visualization to support intraoperative decision-making during brain tumor resection

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Abstract

Purpose 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. We present a new visualization software that supports qualitative and quantitative exploration of the effectiveness of a broad range of methods for communicating uncertainty. We expect that the ability to visualize uncertainty during surgery will help surgeons better understand uncertainty in neuronavigation and make more informed decisions.

Methods We developed UVisExplore, a software module for exploring various visualization techniques for understanding the spatial distribution of uncertainty in image registration. UVisExplore incorporates multiple classic uncertainty visualization techniques and introduces two novel paradigms appropriate for surgical environments. We also introduce a novel game-based approach to evaluate visualization effectiveness before surgery. The game scenario emulates the cognitive decision-making process during tumor resection allowing quantitative evaluation of visualization effectiveness in a non-threatening environment while training neurosurgeons to better understand uncertainty.

Results Six clinicians and three computer scientists participated in a study using our game. Participants explored different uncertainty visualization techniques in a tumor resection task and provided feedback. Surgeon-participants preferred *surgeon-centric* approaches, which emphasize uncertainty near the surgical probe. They also preferred explicit numerical measures of uncertainty displayed in millimeters. The game provided valuable insights into uncertainty visualization preferences and interpretation.

Conclusions We provide an open-source 3D Slicer module for visualizing registration uncertainty and a game that allows users to explore uncertainty visualization for tumor resection surgery. UVisExplore provides a platform for exploring and comparing various uncertainty visualization techniques while simulating the decision-making process during surgery. The visualization module and the game proved to be a valuable communication tool and helped narrow the field of candidate visualizations that we plan to test during surgical procedures in the next phase of our research.

Keywords Uncertainty visualization · Registration · Tumor resection surgery

Introduction

The 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 quality of life and survival [1, 2]. To maximize positive 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 in preoperative imaging [3]. However, neuronavigation requires precise alignment (i.e., registration) between the patient's head and the preoperative imaging. Registration errors of several millimeters at the start of surgery are typical [4]. Moreover, the registration accuracy and the validity of preoperative imaging decrease as surgery progresses due to

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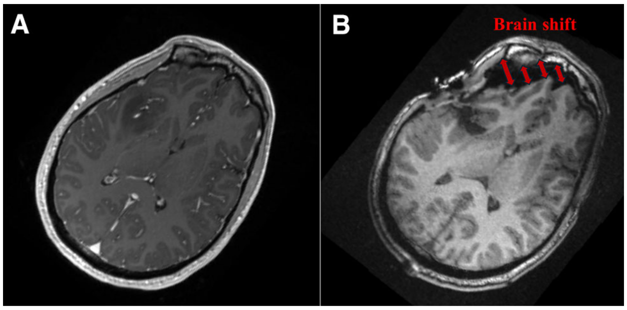

Fig. 1 **a** Preoperative MRI. **b** Intraoperative MRI after brain shift

brain shift and tumor resection, thus introducing additional uncertainty into the localization of neuronavigation systems.

Brain shift

Brain shift is the dynamic and non-rigid deformation of the brain caused by various physical, surgical, and biological phenomena, such as head position, fluid levels and osmotic concentration (Fig. 1). 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 [5].

Brain shift can be compensated by registering preoperative imaging (typically magnetic resonance imaging (MRI)) onto intraoperative imaging, such as MRI [6], surgical cameras [7] or ultrasound (US) [8]. Intraoperative MRI is easily interpreted by neurosurgeons. However, acquiring intraoperative MRI can require 90 + minutes of additional operating room time and is expensive, disruptive to surgery [9], and often not available. Other techniques use intraoperative 2D images from surgical or depth cameras to compensate for brain shift. These techniques register preoperative MRI to the 2D images [7, 10], offering flexibility and low cost but need an unobstructed view of the brain surface and are of limited use during resection. Intraoperative US is an inexpensive and real-time alternative to other imaging techniques. However, US images are difficult to interpret and may not show tumor margins clearly [11, 12]. Multiple methods for registering these different imaging modes to preoperative MRI exist, but all are subject to spatially varying error and uncertainty.

Registration error and uncertainty, even when localized to specific regions, can reduce a surgeon's overall confidence in neuronavigation. Providing a visualization of the spatial distribution of registration uncertainty could help surgeons know where navigation can and cannot be trusted. We hypothesize that this knowledge will increase their confidence in neuronavigation. However, effectively conveying the spatial distribution of registration uncertainty remains a significant challenge. Geshvadi [13] provides a review of relevant literature on visualization in medical imaging, including approaches for both qualitative and quantitative evaluations. Some studies have attempted to provide general methods for visualizing uncertainty [14, 15]. 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.

In this paper, we investigated the gap between existing uncertainty visualization techniques and the practical integration of these methods into the complex surgical environment. This complexity, and the diversity of personal preferences among surgeons, exposed a need for tools to explore, customize, and evaluate uncertainty visualization methods. Thus, we developed UVisExplore, a Python-based software module in 3D Slicer [16] for this purpose. We also introduce a novel game-based approach for evaluating the effectiveness of these uncertainty visualization methods. Our goal is to help surgeons effectively understand the concept of uncertainty and make more informed decisions.

Contributions

1. We introduce two novel uncertainty visualization paradigms specifically tailored for intraoperative tumor resection: *surgeon-centric* and *tumor-based* uncertainty visualization.
2. We present UVisExplore, a software system for exploring a broad range of uncertainty visualization methods, including classic methods, surgeon-centric, and tumor-based methods. The system facilitates interactive exploration of individual methods and their parameters and of combinations of these methods. This software is available under an open-source software license at (link-to-be-provided-on-acceptance).
3. We introduce the use of game-based approaches for quantifying the effectiveness of uncertainty visualization. We provide a game which simulates the decision-making process during tumor resection in the presence of registration uncertainty.

Methods

Exploring uncertainty visualization

Visualization module

UVisExplore is implemented as a custom Python module in 3D Slicer [16], an open-source medical image visualization platform. UVisExplore allows users to explore a variety

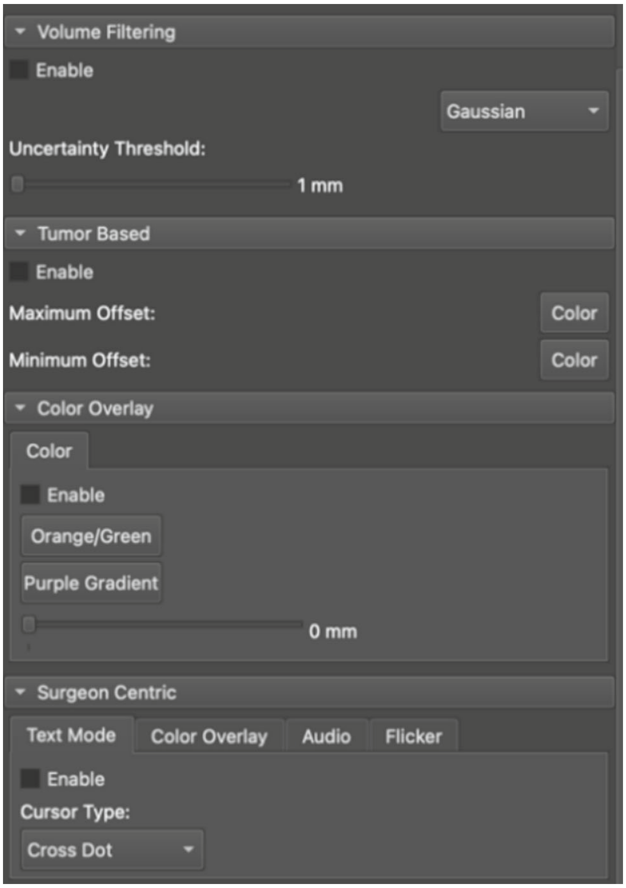

Fig. 2 User interface screenshot

of uncertainty visualization methods and method features. Based on feedback during interviews with neurosurgeons and literature review (e.g., see [13]), we selected variable features for each method (Fig. 2).

Four different visualization categories are: classic 1) Color overlay (Fig. 3) and 2) image filter-based methods (Fig. 4) and our novel 3) Tumor-Based and 4) Surgeon-Centric methods. Features are controlled with sliders and checkboxes.

Tumor-based methods visualize uncertainty using 'error bars' around the tumor boundary by drawing both minimum and maximum offset surfaces predicted by the registration uncertainty along the boundary (Fig. 5). It reveals a safe zone inside the minimum offset surface where surgeons can operate with confidence. Grigoryan et al. [17] provide a similar visualization of boundary uncertainty using color maps.

Surgeon-centric methods

Focus the uncertainty visualization where the surgeon is most interested, i.e., at the tip of their surgical instrument in the navigation system (Fig. 6). This is similar to the sensitivity lens of Lundström et al. [18]. We investigated four different surgeon-centric modes designed for tumor resection surgery:

- *Text mode* displays registration uncertainty at the tooltip as a graphical overlay. The uncertainty can be visualized as a numerical measurement (e.g., 6 mm) or encoded in the size or shape of the cursor (Fig. 6A and B).
- *Color overlay mode* uses classic color overlay methods but restricts the visualization to a sphere surrounding the instrument (Fig. 6C).
- Auditory mode gives verbal warnings in high-uncertainty regions.
- *Flicker mode* causes the image to flicker when the instrument moves into unsafe regions.

Understanding user preference—qualitative evaluation

Evaluating the effectiveness of uncertainty visualization is challenging because uncertainty is intuitively communicated and is inherently related to probabilities. It is also essential to assess its effectiveness under realistic conditions [19]. We evaluated the effectiveness of the visualizations both qualitatively and quantitatively.

For qualitative studies, we used an iterative design process for exploring user preferences for uncertainty visualization. We initially discussed our motivation with two neurosurgeons, refined it based on their input, and presented multiple uncertainty visualization method initial prototypes and obtained feedback through informal interviews and questionnaires. During demonstrations, we invited neurosurgeons to express their ideas and insights regarding their perceived effectiveness using the think-aloud protocol [20]. This provided insights into what worked well and what did not, helping us refine the visualization features.

We presented UVisExplore to a group of 15 subjects, including one neurosurgeon, one medical doctor, three senior image-guided neurosurgery researchers and ten junior researchers with computational and/or pre-medical backgrounds. We presented the system and showed examples of the various visualization modes and features. Subjects were asked to fill out an online survey during the presentation. Questions in the survey were designed to record the subjects' impressions about how useful and intuitive the various methods and features were. At the end, the survey asked subjects for their preferred methods or combination of methods and posed an open-ended question for additional suggestions.

Game-based evaluation of uncertainty visualization

Ultimately, novel technologies for surgical guidance must be tested and evaluated in the operating room. However, focus on patient care and critical decision-making leave little

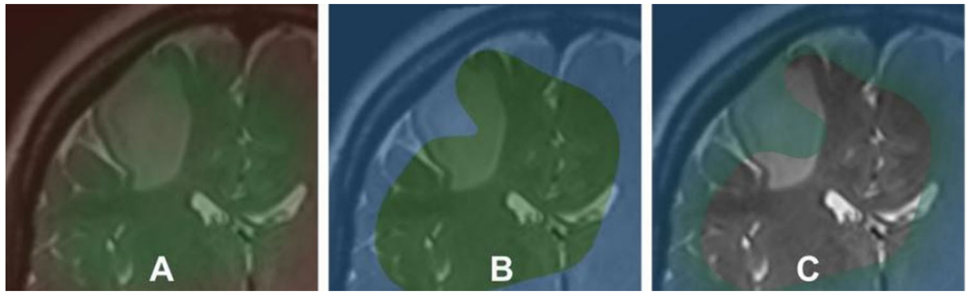

Fig. 3 **A** Color overlay (red indicates high uncertainty, green low). **B** A binary visualization to categorize uncertainty based on a user-selected threshold (e.g., above 3 mm of uncertainty). **C** The color overlay can be visible only when the uncertainty is above the user-selected threshold

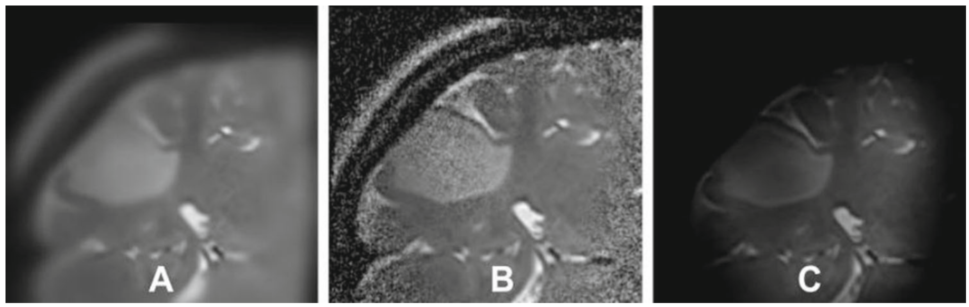

Fig. 4 Image filtering methods: **A** Applies Gaussian blur based on local uncertainty. **B** Adds white noise where uncertainty is higher. **C** Adjusts transparency based on local uncertainty

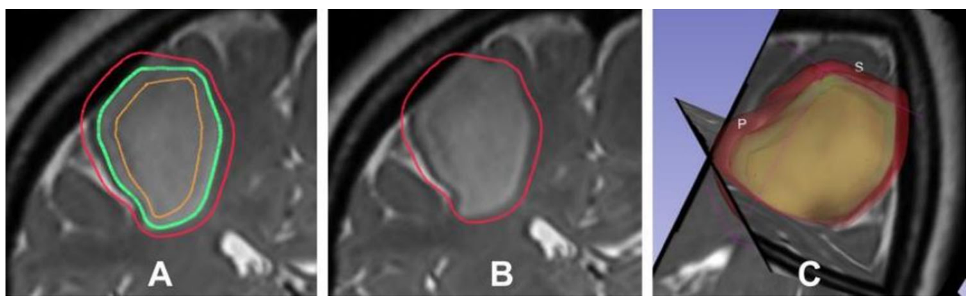

Fig. 5 **A** Tumor boundary (green) with offset boundaries (red, yellow) based on local registration uncertainty at the segmented boundary. **B** Red boundary shows maximum tumor extent. **C** 3D view displays 3D offset surfaces

time for iterative exploration of user preferences and performance evaluation. To provide more controlled and less stressful environments, we introduce the concept of using games to evaluate uncertainty visualization. A game can provide realistic situations for learning about uncertainty and understanding its impact on surgical decisions. Users can explore various visualization methods, features, and combinations and chose those that suit their preferences and the demands of the game. The game provides a backdrop for communication between user and researcher while offering a compelling, competitive activity that encourages users to stay engaged.

We developed a computer game for evaluating registration uncertainty visualization during brain tumor resection in the presence of brain shift. The user is presented with a preoperative MRI image after it has been deformably registered to intraoperative imaging. The system has a corresponding map of spatially varying uncertainty of the deformable registration. The user is asked to virtually resect tumor from

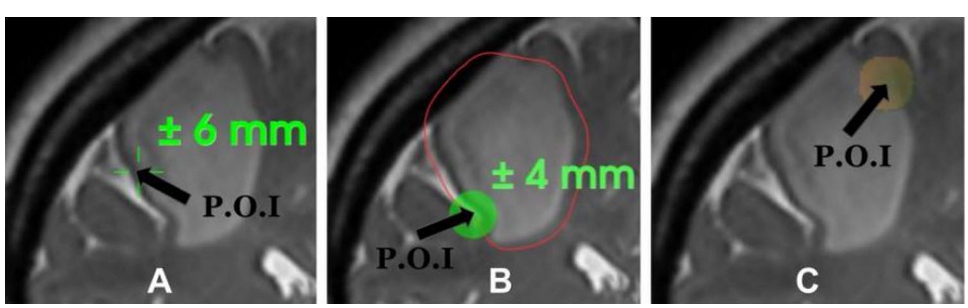

Fig. 6 Surgeon-centric methods visualize uncertainty near the instrument via **A** uncertainty in millimeters, **B** a resizable cursor, or **C** a localized color overlay

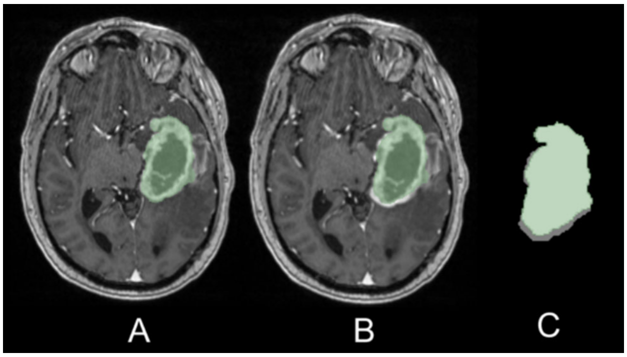

Fig. 7 Brain Image Deformation **A** the preoperative image and planned resection (in green) after (imperfect) deformable registration to intraoperative imaging. This is the image seen by the game player. **B** shows the true registration according to a simulated deformation-uncertainty generation. **C** highlights the difference between the true tumor boundary at the time of intraoperative imaging and the boundary predicted by the (imperfect) deformable registration

the image with and without visualization of the registration uncertainty. This game allows users to set visualization parameters.

Data

Figure 7 shows sample image data from a clinical case used in our game. In a clinical situation, the true deformable registration is unknown (otherwise the uncertainty would be zero). There are methods for simultaneously estimating registration and uncertainty. However, it is still an open question as to how to validate the predicted uncertainties. For this reason, our game used simulated deformation and uncertainty pairs. Simulation allowed us to define 'known' deformable registration and then to generate corresponding registration uncertainty and predicted deformable registration for use in the game. This approach provided known ground truth registration and uncertainty maps to support quantitative evaluation.

We utilized preoperative images of contrast enhancing brain tumors from the ReMIND dataset [21]. Specifically, we select post-contrast T1 scans with manual delineations of the tumors. From this dataset, 2D axial slices showing brain tumors were selected from clinical datasets. To simulate deformable registration and its corresponding uncertainty, we generated an uncertainty map using Perlin noise [22]. Perlin noise, known for its structured and locally smooth characteristics, has previously been used to simulate resection cavities [23]. To mimic realistic conditions where brain shift does not affect the skull, the displacement field is set to zero outside the brain. As most deformations are expected to occur near the tumor due to tissue resection, retraction, and other surgical maneuvers, we multiplied 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 scaled the Perlin noise to define maximal displacements in millimeters to 4 mm. This rescaled Perlin noise is considered an upper bound of the displacement field associated with the residual registration errors. The uncertainty map was then generated by calculating the Euclidean distance of this upper bound in millimeters. We then created 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 ensured that registration error is upper-bounded by the uncertainty.

Finally, we created a triplet of images comprising 1) a registered image that compensates for brain shift but is subject to registration error; 2) an uncertainty map showing the distribution of uncertainty in the registration error, which indicates the upper bound of uncertainty; and 3) a registration error map showing the actual registration error as ground truth. This triplet provided a comprehensive dataset for users to explore uncertainty visualization and ground truth measurements could be used for quantitative evaluation.

Object of the game

The goal is to resect tumor as completely as possible without removing healthy tissue. Players are presented with the imperfectly registered preoperative image and (sometimes) with a visualization of the registration uncertainty map. Players know that the registration is imperfect and that they can use the uncertainty map to guide their decision-making about whether to resect at a particular location (for example, to avoid resection in regions near the tumor boundary where uncertainty is high).

Scoring

Players receive positive points for every true tumor pixel erased. They receive negative points for every pixel outside the tumor erased (Fig. 8). The final score is a weighted sum of these positive and negative points; typically, negative points are given larger weights to emulate the importance of preserving healthy tissue.

Gameplay

Preliminary setup

A 5-min tutorial explains that the preoperative image has been deformed to match intraoperative imaging but that the deformable registration is imperfect and has an associated spatially varying registration uncertainty. The available uncertainty visualization modes and features are explained and demonstrated. The order that these modes are presented

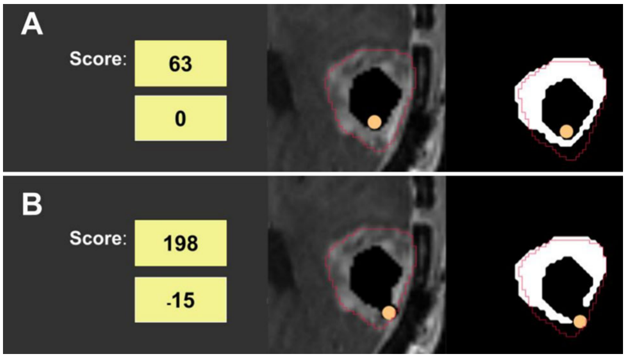

Fig. 8 The orange tip indicates the user's resection tool, and the black area shows the resected region. **A** When the tip is within the true tumor, the user earns points. **B** When resecting outside the tumor, loses points

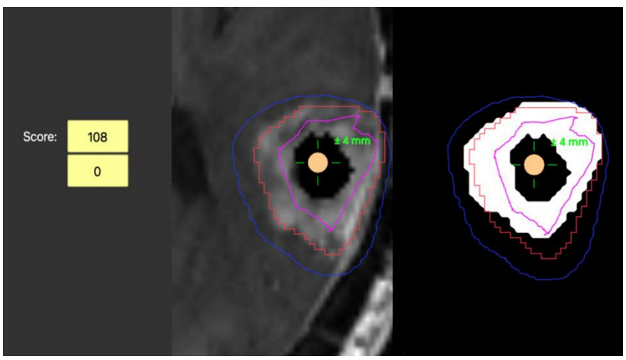

Fig. 9 Training level: Users can view the actual registration error distribution (shown in white) and their real-time scores. This example includes both tumor-based and surgeon-centric text mode visualizations

was randomized to prevent bias. Players are then presented with a first deformably registered image and its registration uncertainty map. They are encouraged to explore different visualization features.

Training level

The purpose of this level is to introduce players to the goal of the game, the gameplay, and the concept of uncertainty. In this level, players can see the ground truth deformation and their negative and positive scores to understand the effects of their decisions while playing (Fig. 9). Players resect tumor by moving their computer mouse over the area they want to resect. Training time is limited to provide equal practice time for players. Players are allowed to continue to explore and customize and change their selected visualization during the training level. At the end of this level, their final visualization choice is fixed and used in the next level.

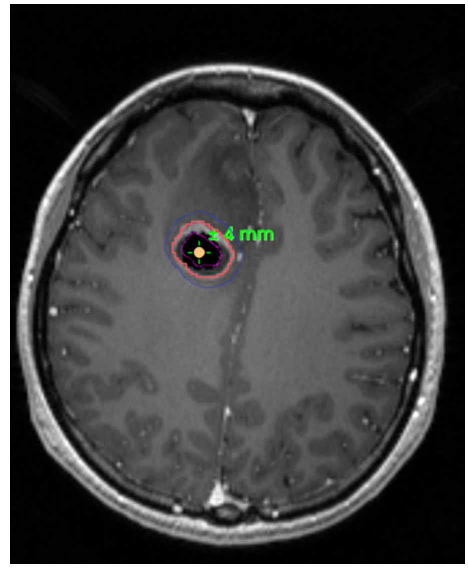

Fig. 10 Challenge level: Users only see the uncertainty visualization they selected and do not have access to scores or the actual registration error distribution

Challenge level

The second level more closely emulates real tumor resection, where surgeons do not necessarily know if the tissue they are resecting is tumor or healthy tissue. Thus, in this level, players cannot see their scores, or the ground truth images (Fig. 10). No undo option is provided, so players need to resect critical areas with care.

Players perform the challenge twice: first without visualization to establish a baseline of what they would resect with just knowing that the registration was imperfect. Second, players perform the resection on the same dataset but with uncertainty visualization. Positive and negative scores with and without visualization are revealed after both attempts at the challenge level.

Evaluation

We performed a study in which five neurosurgeons, one medical doctor without neurosurgery training, and three computer scientists used our game in the presence of a researcher. During the preliminary setup and training levels, the researcher recorded player comments and feedback about the visualization techniques, observed how the techniques were explored, and recorded the mode, features, or combination of modes that the player selected for the challenge level.

Table 1 Uncertainty Visualization selection for participants

Participant #	Selected Uncertainty Visualization Technique
1	CO + SCTM
2	CO + TB
3	SCTM + TB
4	SCCO + SCTM + TB
5	CO + SCTM + TB
6, 7, 8, 9	SCTM + TB

Participants 1–3: computer scientist, Participant 4: MD without neurosurgery training, Participants 5–9: neurosurgeons. CO = Color Overlay, SCTM = Surgeon Centric Text Mode, SCCO = Surgeon Centric Color Overlay, TB = Tumor Based.

Results

Exploring uncertainty visualization

Our subject survey showed that tumor-based visualizations were selected as the most intuitive. Regarding usefulness, 53% of subjects specified tumor-based methods. The neurosurgeon pointed out that the most helpful visualization method depends on context (e.g., during presurgical planning, during tumor resection, or during a time-out during surgery) and emphasized the need for a customizable tool. Many subjects made valuable suggestions which we used to enhance UVisExplore. In addition, users expressed a strong desire for the ability to control visualization features and the need for interactive exploration of modes, mode combinations, and features.

Game-based evaluation of uncertainty visualization

Table 1 shows what game players selected for uncertainty visualization after the training level. 88% of participants included tumor-based modes, and 88% included text modes. All of the neurosurgeons selected a combination of tumor-based and text-based modes. One of them also used a color overlay. 77% explored multiple techniques during the training level and chose their final 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 useful thresholds for these modes.

The selection of tumor-based and text modes by all the neurosurgeons highlights the effectiveness of our novel techniques. Neurosurgeons were most interested in uncertainty visualization centered on the surgical probe, with the tumor boundary being the most critical area for uncertainty visualization. When asked if they would use their selected visualization technique in the operating room, 80% of the neurosurgeons responded in the affirmative.

We hypothesized that players would achieve higher positive scores and lower negative scores with uncertainty visualization. All non-neurosurgeon participants received fewer negative scores with uncertainty visualization. Since negative scores reflect the resection of healthy tissue, reducing negative scores is particularly important. Therefore, the uncertainty visualization appears to improve decision-making for non-neurosurgeons (Table 2).

The results were more mixed for the neurosurgeons (participants 5–9). Only 40% of surgeons improved their overall scores, and only 40% reduced their negative scores.

In post-game interviews, 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 and less conservative where excessive resection was not critical. A third clinician dismissed the uncertainty map altogether because it did not fit their knowledge and experience. In particular, they expected the direction of brain shift to follow gravity and they expected higher uncertainties inside the tumor and lower at the skull. Their skepticism biased them against the game from the start. This feedback was very important as it reflected that our Perlin noise-based simulation failed to take anatomy and physics into account; future versions of the game can account for these biophysical effects.

Discussion and conclusions

We present UVisExplore, a software system designed to explore, teach, and evaluate a broad range of techniques for visualizing registration uncertainty during tumor resection surgery. We developed UVisExplore to address the need for an easy-to-use tool for exploring visualization methods in real and simulated environments. We used UVisExplore to teach clinicians about uncertainty visualization and to gather user feedback. 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

Table 2 Level 2 Game Scores

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

(participant roles as in Table 1). The best possible score: 404 positive and zero negative.

learned several things that we plan to use to improve our game for future work.

One limitation of our work is that neurosurgeons were not involved in selecting specific cases or deformation models for our experiments. As a result, we found that some of the simulated tumor deformations are not physically realistic. In future work, we plan to develop simulations that incorporate typical properties of brain shift and that respect anatomical constraints. These insights highlight the importance of considering neuroanatomy when deforming the image and of close collaboration with neurosurgeons to ensure that images are clinically relevant and that simulations are intuitive. We learned that uncertainty is more significant in critical areas, such as motor function and language regions, where surgeons will perform more conservative resections. We plan to add cost functions to our scoring system that weigh critical regions more heavily than non-critical regions. 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 important new direction for evaluating uncertainty visualization.

One limitation is the difficulty in accurately simulating the complexity of brain tumor surgery in a 2D game model. High-grade brain tumors often have infiltrative components that extend beyond the gadolinium-enhancing margins, and the extent of safe resection is determined by numerous factors. Furthermore, brain shift is a multifactorial process influenced by skull opening, tissue manipulation, edema, microhemorrhages, and other intraoperative factors that develop with varying intensity and timelines. We do not attempt to predict all deformations. While intraoperative ultrasound and MRI can mitigate uncertainty to some extent, there will always remain some uncertainty. It is important that surgeons understand and appreciate this uncertainty during intraoperative decision-making. This tool cannot begin to model the complexity of tumor surgery, but it can allow surgeons to explore and understand the concepts of uncertainty in navigation in a controlled and safe environment.

In future, we plan to add more levels to our game and include a more diverse set of tumor images, and we also plan to develop a 3D version of the game. We aim to make the next version more dynamic, with the brain shift occurring over the course of the tumor resection, and we plan to improve simulation accuracy and explore different surgical scenarios, such as during presurgical planning, tumor resection, or a time-out during surgery, where different visualization techniques might be more or less valuable. We plan to use UVisExplore and our game-based approach as a training tool for neurosurgeons and neurosurgical residents to teach them about uncertainty and improve their understanding of it. Ultimately, we plan to begin evaluating uncertainty visualization in real surgical settings.

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Declarations

Conflict of interest The authors have no competing interests to declare.

Ethics approval This study was approved by the Institutional Review Board (IRB) of Brigham and Women's Hospital.

Informed consent This article does used patient data from a public database under IRB approval.

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