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Semi-autonomous Image-guided Brain Tumor Resection using An Integrated Robotic System: A Bench-Top Study

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Abstract

Background—Complete brain tumor resection is an extremely critical factor for patient's survival rate and long term quality of life. This paper introduces a prototype medical robotic system that aims to automatically detect and clean up brain tumor residues after the removal of tumor bulk through conventional surgery.

Methods—We focus on the development of an integrated surgical robotic system for image-guided robotic brain surgery. The Behavior Tree framework is explored to coordinate cross-platform medical subtasks.

Results—The integrated system was tested on a simulated laboratory platform. Results and performance indicate the feasibility of supervised semi-automation for residual brain tumor ablation in a simulated surgical cavity with a sub-millimeter accuracy. The modularity in the control architecture allows straightforward integration of further medical devices.

COMPETING INTERESTS

Eric J. Seibel and Blake Hannaford participate in royalty sharing with their employer, the University of Washington, which has ownership of patents that may gain or lose financially through this publication. Blake Hannaford is a co-founder of Applied Dexterity Inc. which manufactures and markets the RavenTM II surgical robotics research platform.

Conclusions—This work presents a semi-automated laboratory setup, simulating an intraoperative robotic neurosurgical procedure with real-time endoscopic image guidance and provides a foundation for the future transition from engineering approaches to clinical application.

1. INTRODUCTION

Ever since the first documented robotic-assisted surgical procedure in 1985 [1], when an industrial robotic arm (PUMA 560) was used for neurosurgical biopsy, surgical robotics has been studied and developed for many medical applications by many research groups worldwide. In the last decade, new medical imaging and image-guidance technologies have been explored in combination with robotics to augment a variety of medical procedures by providing surgeons with accurate spatial information about the location and anatomical relationships of subsurface structures and instrument positions [1]. This integrated technology of medical imaging, image processing and segmentation, registration, tracking, and visualization, as well as human-robot interaction offers potential benefits to both patients and physicians, and thus has been intensively studied and applied primarily in minimally invasive surgery. Clinical applications using image-guided robotic technology show enhanced dexterity and precision during the operation in the area of urology [3], orthopedics [4] and neurosurgery [5], [6], compared to the traditional open or laparoscopic surgery, although an evidently improved outcome of the robotic surgery has yet to be seen. In the past few years, the development of molecular imaging technologies has greatly increased the visual information available to the surgeons during the operations. Fluorescence imaging has been shown feasible during cancer surgery (i.e. tumor resection) using available imaging systems and contrast agents [7], and has the potential to reduce the frequency of positive margins and the number of second surgeries [8], [9].

1.1. Clinical scenario and medical problem

For patients with malignant gliomas, a greater extent of resection of the brain tumors is the key to the higher survival rate. Clinical study of patients with glioblastoma showed significantly longer survival times for patients with 98% or more resection of tumor volume [10]. However, complete resection of the brain tumor at the margins is still a challenging task for surgeons due to the lack of clear delineation between the tumor tissue and normal brain tissue in real time and the complex anatomic situations with high-risk structures in the brain. Therefore, complete resection can only be achieved in a minority of patients. Recently, tumor material has been visually enhanced by modern contrast agents. One such agent, 5-aminolevulinic acid (5-ALA) has been assessed in many clinical studies [11], [12]. “Tumor Paint” or BLZ-100 is another tumor-specific fluorescence for indicator for brain tumors [8] and other select tumors [14]. It is able to selectively bind to brain tumor cells and fluoresce in the NIR with the molecular dyes, cyanine5.5 [13] or indocyanine green [9] (Fig. 1).

Because fluorescence responses of residual tumor cells remaining after the major debulking can be very weak, a significant long integration time may be required for a clear image segmentation. Due to this long integration time, manual treatment of the smallest fluorescently labeled tumor residues is very tedious and nearly impossible. Thus, this

procedure for tumor residue ablation is ideal for robotic automation with advanced multimodal laser-based imaging.

Based on the above clinical scenario, we explore the feasibility for robotic automation of residual brain tumor resection under surgeon's supervision. It is assumed that the bulk of the brain tumor will be removed through conventional surgery and a surgical cavity up to a ping-pong ball size will be exposed afterwards. Our goal is to automatically detect and clean up the tumor residues exposed and remaining on the wall of the surgical cavity using an intelligent robotic system, which is envisioned with a RAVENTM II-based, fluorescence-guided and surgeon-assisted system of the future described in Fig. 2, with one or more robotic arms that hold a multimodal Scanning Fiber Endoscope (SFE) described in Fig. 3, and a surgical suction tool for removing blood and/or ultrasonically driven tool to resect brain tissue.

This paper describes a bench-top implementation of the robotic automation of a neurosurgical procedure for excavating the brain tumor residues under surgeon's supervision. Phantom tissue, glutinous "tumor" material, and visible light color segmentation are used in this bench-top study. The automated surgical procedure is divided into six subtasks as listed below, performed sequentially.

1. Collection of medical images: scanning of the surgical cavity exposed after manual debulk
2. Medical image processing:
 - a. 3D reconstruction of the surgical cavity
 - b. Tumor residues localization in the surgical cavity
3. Generation of ablation plan
4. Plan selection by the surgeon
5. Robotic execution of the plan with vision feedback
6. Validation of the ablation outcome via SFE vision

These subtasks will be repeated until no cancerous tissue is detected in the last step. Algorithmic details of subtasks will be addressed in the following sections. In the earlier papers, we have showed the feasibility of modeling the ablation procedure using the Behavior Tree framework [15] and creating a 3D mosaic using a set of 2D reflectance SFE images [16], as well as the validity of a surgical coverage path planner based on the pre-known point-cloud of tumor residues [17] individually on the robotic system and SFE imaging system respectively. The RAVENTM II surgical robotic software is implemented in C/C++ on a real-time patched Linux system, while the SFE imaging system was originally developed in LABVIEW® and MATLAB® on a Windows system that required manual operations for image acquisition. To achieve the robotic automation of a medical procedure, the information/data flow between all medical systems needs to be automated too. This paper is built upon the above publications with updates and reimplementation. Particularly, we focus on integrating an intelligent surgical robotic system on software and hardware level, as well as development and validation of the algorithms for medical imaging and

guidance of surgical instruments subject to medical procedure constraints and real-time endoscopy. New software modules are implemented and incorporated into a three-layer control architecture to realize the automatic control of the proposed surgical procedure. Finally, a simulated experimental setup is designed and tested using the proposed surgical system. Performance analysis of the semi-automated brain tumor resection procedure is given and discussed at the end. Surgical scenario is a complicated environment which oftentimes comes with a lot of challenges such as wet surfaces, bleeding, tissue motion and tissue deformation. Possible robotic solutions to part of these challenges are provided in the discussion section for the further development of the robotic medical system. In this paper, we aim to provide a pilot study of an integrated intelligent medical robotic system for semi-automation of a medical procedure in image-guided brain tumor ablation surgery.

2. MATERIALS AND METHODS

2.1. Control architecture

The entire framework is implemented using the ROS API (www.ros.org) on Linux systems. The communication among different Linux machines and across different layers is established based on ROS Message and Action protocols. The top layer is a Behavior Tree (BT) that models the medical procedure for brain tumor resection. The middle layer consists of functional modules that prepare and process the corresponding data requested by the BT. The bottom layer contains a set of control modules which directly control the driver of each hardware system. The control architecture is depicted in Fig. 4. The 3D image reconstruction module is implemented as a ROS Action server. The automatic SFE image grabbing is implemented as a control module at the bottom layer. These new modules will be explained in detail in the following sections. The top layer behavior tree has been updated to cope with the expanded functionalities. A modified version of the BT is shown in Fig. 5. Each medical subtask is hardcoded into an action node (green round circle). Five new BT action nodes (scanning, 3D reconstruction, tumor localization, execution, and check) are implemented, expanded from [15]. Five types logic nodes are used for transition between different subtasks. They are one recovery node (circular arrow ↺), three sequence nodes (rightwards arrow →), one decorator (diamond ♦), one selector (question mark ?) and one parallel node (rightwards paired arrows ⇨).

2.2. Automatic acquisition of endoscopic images

The SFE imaging device is controlled from a LABVIEW® interface in a Windows PC. Data transfer between the PC and the SFE control box is based on the PCIe serial protocol. In the previous work, manual operations were required on the LABVIEW® interface to save the SFE images into the local disk for further image processing. To integrate this operation with the existing control architecture for automatic robot intervention, a new module for SFE image frame grabbing and publishing onto the network in ROS Message is implemented. The Epiphan® frame-grabber is used as an intermediate for image data conversion. Fig. 6 shows the systematic control flow among the different devices such that the SFE images can be accessed seamlessly by other software modules any time when needed without manual operation.

2.3. 3D image reconstruction of the surgical cavity

Endoscopic imaging has become an essential component in minimally invasive robotic surgery as it provides surgeons with visual information to precisely localize lesions in a complicated anatomic environment. Analysis of these diverse types of images for 3D information extraction requires sophisticated computerized quantification and visualization tools. Stereo-endoscopes have become available in recent clinical applications to provide direct 3D information of a surgical scene. Algorithms with GPU or hybrid CPU-GPU enhancement have greatly improved the reconstruction speed and allowed dense intraoperative surface reconstruction of soft tissue in real time from stereo endoscopic images [18], [19]. Although 3D stereo-endoscopes may provide the surgeons with better visualization experiences compared to the conventional 2D endoscopes, they are significantly more expensive. An alternative approach based on Structure from Motion (SfM) techniques originating from robotic vision have given the conventional monocular 2D endoscopes 3D capabilities.

The essence of the structure from motion algorithm is pairwise 3D reconstruction between the neighboring images where the feature tracking is dense and reliable but with sufficient special difference between the images for robust triangulation. Traditional feature detection algorithms have been applied to find the correspondence in an image pair. In [20] the authors used an optical flow algorithm to harvest 3D features from 2D endoscopic images; in our previous paper [16], the Scale-invariant feature transform (SIFT) feature tracker (computationally expensive but presumably with better performance) was used to find the vascular feature points in a surgical cavity. In this paper, feature points are tracked using Oriented FAST and Rotated BRIEF (ORB), which uses Features from Accelerated Segment Test (FAST) in pyramids to detect the features and finds their orientation using first-order moments and computes the descriptors using Binary Robust Independent Elementary Features (BRIEF). ORB uses the binary descriptor BRIEF and thus is much faster, compared to SIFT and SURF, which are gradient based descriptors and computationally more expensive.

2.3.1. Reflection removal—SFE imaging in the wet surgical environment usually results in strong specular reflections in the image, which degrade the reconstructed 3D model due to the false detection of high contrast feature points. To improve the robustness of reconstruction, those saturated reflection points were removed in the SFE images first before feature detection. The specular reflection in the SFE images is displayed as saturated pixels. A binary mask is created from these saturated pixels. The color information in the mask is then restored from the neighboring pixels based on image inpainting method. Fig. 7 compares the same SFE image before and after reflection removal. Although not all color information can be recovered inside the specular reflection regions, these false features cause by the specular reflection are safely pruned. The processed SFE images are the inputs for the 3D reconstruction pipeline.

2.3.2. 3D reconstruction pipeline—Fig. 8 describes the pipeline of the reconstruction module. This module executes the reconstruction procedure when requested by an action client node in BT using ROS Action protocol and sends the generated point-cloud of the

surgical cavity back to the client node on completion of the process. The implementation is based on the OpenCV (www.opencv.org) library for image processing and the SSBA library for bundle optimization. Feature points in each endoscope image are detected using the ORB algorithm. These feature points are matched in pairs and validated through the Random Sample Consensus (RANSAC) algorithm as shown in Fig. 9. The depth of each matched feature point is then recovered through triangulation. Last steps are optimization of the 3D points and camera parameters using bundle adjustment and smoothing of the generated 3d model.

2.3.3. Performance improvements—It is shown that the performance of reconstruction algorithm has significantly improved compared to the previous results [16]. The runtime is about 20 times faster based on solely CPU computing, and this speed can be further improved by enabling GPU computing capability. Furthermore, the recovered point-cloud of the surgical cavity is about 10 times denser. Technical specifications of the 3D reconstruction algorithm are given in Table 1.

2.4. Tumor residue localization

In the last step, we generated a set of points that represent the surface geometry of the surgical scene. However, these points do not necessarily contain the points of green residual tumor cells in the phantom. The goal of this step is to recover 3D point-clouds, $\mathbf{P}_t$, that represent the tumor residues, from SFE poses, 2D pixel segments $\mathbf{P}_{\text{pixel}}$, and a 3D point-cloud of surgical cavity $\mathbf{P}_s$ from the last step. The physical relationship of these input parameters is depicted in Fig. 10. This procedure is further divided into four steps:

1. create the mathematical surface model from $\mathbf{P}_s$ using Thin Plate Spline (TPS) interpolation.
2. determine the ray function for each segmented tumor pixel.
3. compute the intersection point between the ray function and surface model.
4. cluster point- clouds from each image segment.

Fig. 11 describes the block diagram of tumor residue localization. In the following, details of each step are explained.

2.4.1. Thin Plate Spline based surface model—Thin Plate Spline (TPS) [21] is a spline-based surface fitting technique. It has been widely used as a non-rigid transformation for shape warping because it is insensitive to the noise of the data set. A physical analogy of TPS is to bend a piece of thin metal sheet. TPS fitting uses a set of weights to describe the smoothness of the fitted surface by minimizing the bending energy. More precisely, we need to find a mapping function $f: (x_i, y_i) \rightarrow z_i$ from the point set $\mathbf{P}_s$ by minimizing the following energy function (Eq. 1) such that any arbitrary point on the fitted surface can be computed from the projection on the world XY plane of the same point.

$$E_{TPS}(f) = \sum_{i=1}^n \|z_i - f(x_i, y_i)\|^2 + \lambda \iint \left(\left(\frac{\partial^2 f}{\partial x^2} \right)^2 + 2 \left(\frac{\partial^2 f}{\partial x \partial y} \right)^2 + \left(\frac{\partial^2 f}{\partial y^2} \right)^2 \right) dx dy \quad (\text{Eq.1})$$

where $\lambda = 0$ is a pre-defined regularization parameter that measures the goodness of the fitting. For $\lambda = 0$, the TPS surface is reduced to a plane using least square fitting indicating zero bending energy. We choose $\lambda = 1$ empirically based on the overall smoothness and fit of the original point-cloud $\mathbf{P}_s$.

The coefficients of the mapping function can be solved uniquely in closed-form by inverting a non-singular matrix of size $(n+3) \times (n+3)$, where n is the number of the points in $\mathbf{P}_s$. This operation leads to a complexity of $O(n^3)$ and becomes slow when the point-cloud $\mathbf{P}_s$ gets large. Many studies have reduced the computation cost by different methods, e.g. [22] used a preconditioned conjugate gradient method to solve the system of equations; [23] proposed optimal low-rank approximations to TPS that were both computationally efficient and stable. In our case, we use QR decomposition to perform the matrix inversion. The computation time is about two seconds when solving for about 2000 points, which is still tolerable when compared to executing time of the entire medical procedure.

2.4.2. Determination of the ray function—The physics of SFE imaging is approximated as a pinhole camera model for simplification. Each 3D point in space is projected uniquely on the projection plane at a certain pixel location. From the mathematical relationship, a 3D point representing the tumor cell must lie on the line which connects the camera optical center and the corresponding pixel point on the projection plane as depicted in Fig. 10. We define the mathematical representation of this line in world frame as a ray function in Eq. 2.

$$f_{ray} \triangleq \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} x_c \\ y_c \\ z_c \end{bmatrix} + t\mathbf{R} \begin{bmatrix} \frac{u-c_x}{f_x} \\ \frac{v-c_y}{f_y} \\ 1 \end{bmatrix} \quad (\text{Eq. 2})$$

where $[x_c, y_c, z_c]^T$ is the location of SFE optical center in the world frame. Rotation matrix $\mathbf{R}$ transforms a point in the SFE frame to the world frame. $[u, v]$ is the pixel location on the image and $[c_x, c_y]$ is the principal point. $[f_x, f_y]$ are the focal lengths along the camera x and y axis respectively.

2.4.3. Computation of the intersection point—The location of a tumor cell in space must satisfy two constraints: 1) ray function and 2) TPS mapping function. For each pixel segmented from the fluorescence image, there is a unique corresponding 3D point in space representing the tumor cells, i.e. the intersection point between the ray function and TPS surface determines the 3D location of tumor cells detected in the endoscopic image. A numerical method is used to search for the intersection point iteratively. We start with two initial points on the ray function: SFE position $p_1 = [x_c, y_c, z_c]^T$ and the intersection point between the ray and the world XY plane $p_2 = [x', y', 0]^T$. Note that p_1 must not be on the TPS surface while p_2 could be on the surface, in which case the iteration finishes in one loop with p_2 as the result. There are two possible relations regarding the location of these two initial points when not on the TPS surface. A simplified 2D illustration is given in Fig. 12.

- Case A: two points are located on different sides of the TPS surface (Fig. 12a). In this case, the intersection point is computed by sliding p_1 and p_2 towards each other. The convergence is bi-directional along the ray function. The middle point of p_1 and p_2 will be the intersection point at convergence.
- Case B: both points are located on the same side of the TPS surface (Fig. 12b). In this case, the intersection point is found by sliding both p_1 and p_2 towards the TPS surface for one directional convergence at the point p_2 . Case B can turn into case A after several iterations if $f'_{TPS} f'_{ray} < 0$ when evaluated at the intersecting point.

2.4.4. Points clustering—From the previous steps, we obtain a point-cloud of tumor pieces in each 2D image if tumor residues are detected through segmentation. Each residual tumor may be scanned multiple times in a sequence of SFE images, and thus multiple point-clouds are generated for the same residual tumor. In this step, these point-clouds of the same tumor piece are clustered into a single point-cloud and the ordered contour of the clustered point-cloud is extracted for the automatic generation of ablation plans afterwards. First, we create a 2D grid map on the XY plane of the world frame from the point-cloud of the surgical cavity $\mathbf{P}_s$. Each point-cloud $\mathbf{P}_t$ generated from single fluorescence image is then projected on to the grid map with each grid marked as 1 for tumor and 0 for non-tumor. This step can be interpreted as adding a small tumor patch to the 2D binary map frame by frame. A 2D binary map is created after all point-clouds of the tumor are projected (Fig. 13). The outer contours are extracted since we will treat any holes inside each tumor residue. Finally, the generated contours and corresponding grids inside each contour which represent the tumor cells are projected back onto the TPS surface of the surgical cavity. Hence, in this step, the number of total tumor residues, the contour and the internal points in 3D space of each tumor residue are retrieved, which are the inputs for the path planner.

2.5. Robotic ablation with vision feedback

From the achieved point-clouds of tumor residues, corresponding ablation plans are generated using the path planner described in [17]. The robot will then execute one of the plans approved by the user (surgeon) through a terminal input. We combined two types of vision sources as feedback to improve the overall ablation accuracy: 1) stereo-vision for tracking of the robot position to overcome robot motion inaccuracy. 2) SFE vision for fine adjustment of the ablation path during robotic execution. Here, the second type of vision (i.e. SFE) feedback is addressed.

The obtained 3D model of the surgical cavity might not be accurate enough due to reconstruction errors in the previous step, which sometimes causes over resection observed in the experiment. Moreover, a slight tissue motion might occur anytime during the ablation. In these cases, the generated ablation path becomes inaccurate. Therefore, fluorescence image based feedback is introduced in the ablation procedure for fine adjustment of the robot trajectory to overcome small model inaccuracy and slight tissue motion. Since the SFE is a 2D imaging device, the path adjustment is performed in the lateral plane such that each

via-point in the ablation path is constrained within the tumor area in the 2D image. Fig. 14 illustrates the process of fluorescence image guided path correction during the ablation.

Before the motion command is sent to the robot, the fluorescence image is analyzed. Path correction is only performed when there is a significant amount of tumor visible in the segmented fluorescence image. The target position of the robot end-effector in world coordinate system is projected to the current 2D fluorescence frame to check whether the destination is located within the tumor. All targets which are located away from the tumor area will be corrected towards the tumor. Fig. 15 depicts the three-step correction: 1) project the target 3D point onto fluorescence frame based on the pinhole camera model. 2) compute the centroid of the visible tumor area. 3) compute the intersecting tumor pixel on the line consisting of the centroid and the target pixel. This step is solved by binary search along the line. The intersecting pixel is considered as the adjusted target projection and is reverse-projected back into the 3D world space while preserving the same depth as the old target. Fig. 16 shows the original ablation path and updated path during the execution when treating a round simulated tumor of $\varnothing 6.35$ mm. Due to the reconstruction error, the generated 3D tumor model is slightly larger ($\approx \varnothing 7.21$ mm) than the actual one (green region), as is indicated in the figure that the original path (red dotted line) covers a larger area than the updated path (blue solid line). The proposed algorithm with vision feedback shows a more accurate covering of the tumor area and less normal tissue is removed during the ablation. It is noticed in Fig. 16 that the top part of the path is not corrected due to the lack of visual information because the SFE view of the tumor at this region was blocked by the ablation tool. This problem can be solved if using a higher DOF surgical tool at the robot end-effector to guarantee the SFE vision all time.

2.6. Image verification

After the ablation process ends, an SFE image will be taken 20 mm above the center of the surgical cavity for final analysis (segmentation) to determine whether all tumor residues have been cleaned. Otherwise, another round of the resection procedure will be initiated via a BT recovery node (top logic node denoted in Fig. 5).

3. RESULTS

To validate the above-described methods, a simulated brain tumor residue clean-up scenario is demonstrated. A tool adapter and a surgical phantom are designed and manufactured for the experiment. Results are presented and discussed.

3.1. Design of the surgical phantom

In many medical cases, due to the vague symptoms at the early stage, patients are diagnosed with the brain tumor only when the tumor is very big, similar to the size of a ping-pong ball. Therefore, a phantom in similar size was handmade from layers of the paper to simulate the debulked surgical cavity. A high-resolution brain image from the craniotomy was printed and pasted on the internal surface of the paper cavity. The maximal depth is about 7 mm with a curvature radius of 20 mm as depicted in Fig. 17. A protective film was then applied to the surface of the phantom to create moisture resistance. To simulate the tumor residues,

transparent lotion was mixed with green fluorescence powder, such that this jelly-like mixture can be segmented in visible light, and it can stick to the wall of the cavity and be removed through vacuum suction. In this experiment, the SFE produces images in 3-channel RGB format for 3D reconstruction and tumor segmentation.

3.2. Design of the tool adapter

A tool adapter illustrated in the Fig. 18 was 3D-printed for attaching a suction ablation tube and the SFE to the robot end-effector. Two types of setups (parallel and angled placement of ablation tool and SFE) were tested and worked well. Two set screws were placed perpendicularly for each cylindrical hole to fix the position and orientation of the suction tool and SFE to achieve a minimum bending of the flexible optical fiber. For stereo tracking purpose, three blue markers were placed on a planar surface of the tool adapter such that the poses of the suction tool and SFE can be computed through rigid transforms of the markers. This design allows continuous and robust pose acquisition of the tool and SFE when they are deep within the surgical cavity during the treatment process.

3.3. System setup

A simulated surgical scenario is built upon the RAVENTM II surgical robotic research platform as depicted in Fig. 19. A simulated surgical phantom is placed in the robot workspace. The left arm of the robot is used for the simulated residual tumor resection operation and holds a 7 French suction tool and a Ø1.6 mm SFE. A stereo camera pair is mounted on the base of the robot to provide color-based tracking of the markers, and hence the pose of tool and SFE. Two LED lights are mounted symmetrically around the workspace to create evenly distributed light for tracking noise reduction.

3.4. Creation of a 3d map of the surgical cavity

The proposed ORB feature extractor was able to match a sufficient number of vascular features between the adjacent scans, although the Epiphan® digitizer reduces the image quality significantly. Hence, the generated point-cloud of the simulated surgical cavity was sparse, but dense enough to create a reasonable model of the surface. Fig. 20 illustrates the point-cloud of the surgical cavity along with the detected tumor residue, which is marked in green color. The shape and size of the tumor residue in Fig. 20 match well with the original tumor residue as depicted in Fig. 17a. An average tumor size was computed as $\varnothing 7.23 \pm 0.4$ mm from 10 successive trials when using a $\varnothing 6.35$ mm dot as ground truth. From a set of test trials, we also noticed that the size error of the tumor residue increases with the increasing distance between SFE and surgical cavity due to the increasing triangulation error. Therefore, to achieve a relatively small triangulation error and a robust baseline triangulation, we empirically set the spacing between each SFE image to 4 mm and limited the distance between SFE tip and the surgical cavity to 15 mm. Moreover, the SFE intrinsic parameters play a significant role in the accuracy of the 3D model. Due to the high sensitivity of the SFE, the intrinsic parameters may vary with the force applied on the SFE from set screws and the internal parameter drifting of electronic elements. Hence, at power-up cycle of the SFE system, a manual calibration was executed using SFE control software to reduce the observable central distortion. Multiple conventional calibrations using a checkerboard were performed later and averages of the intrinsic parameters were computed.

Radial and tangential distortion of the SFE images was corrected partially using the calibration results. Some of these average values were then fine-tuned based on a set of test runs. Finally, these refined parameters were used for the 3D reconstruction algorithms.

3.5. Navigation and execution accuracy

The motion control of the suction tool tip and SFE is based on vision feedback and robot inverse kinematics. Direct PID control of desired joint angles is not accurate enough to perform tasks which require sub-millimeter accuracy. Therefore, the stereo-tracking system consisting of two webcams was introduced to provide the ground truth of tool and SFE poses within half mm precision. Fig. 21 plots the position of the SFE and suction tool tip together with the generated 3D point-cloud of the surgical cavity during the execution of a planned resection. The suction tool tip was programmed to move 1.5 mm above the phantom surface to avoid direct contact with the phantom surface. It is shown in Fig. 21 that the tool tip was able to follow the desired treatment path within sub-millimeter accuracy. The robot system RMS error was reported in [17] as 0.207 mm in the stereo-camera frame.

3.6. Procedure duration

The total time duration for the entire semi-autonomous procedure was about 6 minutes. Table 2 lists the CPU time used for each subtask, which is run on an Intel Core™ i7 processor Linux computer with 8 GB RAM. We note that most of the time was used for the two robotic interventions: scan and ablation. Due to the motion blur caused by the video digitizer, extra waiting time is required at the point where SFE saves an image during the scanning procedure. The scanning speed can be further increased by upgrading to a high frame rate stereo pair. The current frame rate is 7.5 Hz due to camera hardware limitation. However, we prefer to keep the tissue removal process slow because on one hand a slow ablation speed helps the suction tool to remove the tissue thoroughly and on the other hand a slower motion of the tool tip prevents big contact forces to the tissue which may cause tissue damage and other unexpected damage in the cranial area with a limited spatial accessibility. For the surgeon, monitoring a slowly moving ablation process with enough time to fine tune the automated surgical procedure or halt an undesired procedure with a foot pedal would be advantageous.

3.7. Success rate

A successful trial is defined as when the integrated system detects all tumor residues, cleans them and passes the visual validation. Table 3 lists the results from 10 trial runs. Each trial used one of the four path patterns to ablate the tumor residue based on its size and shape: zigzag, contour parallel, mix pattern of the both as well as spot-wise suction of small tumors [17]. 7 out of 10 trials were successful. The unsuccessful trials were mainly caused by inaccurate 3D model creation. This is due to several possible reasons. First, the tumor residue is located in a feature-sparse area, which leads to partially inaccurate surface model(#7). Second, the small drifting of SFE internal parameters such as the field of view(#9), as well as the error in bundle adjustment lead to the position error of the 3D model, and hence of the tumor residues. Trial #4 and #7 are not considered as total failure in clinic because the remaining tumor material can be removed in multiple passes as long as there is no damage to the surrounding healthy brain tissue.

3.8. Experiment using wet phantom

To validate the algorithms under a more realistic surgical environment, the phantom was sprayed with water to form a wet surface with strong specular reflections in the SFE imaging (Fig. 7a). A round simulated tumor of Ø6.35 mm was used as ground truth for comparison. Fig. 22 shows a significant improvement in the reconstruction accuracy after removal of specular reflections when using the same set of SFE images. The basic shape of both tumor and the surgical cavity is correctly recovered with reflection removal (right part of Fig. 22).

4. DISCUSSION

This pilot study of the integrated medical robotic system demonstrates the feasibility of supervised semi-automation for brain tumor residue ablation in a simulated surgical cavity. The small size of the high-resolution, wide-field multimodal SFE scope allows the attachment directly on the surgical tool. RAVEN™ II also allows the installations of the surgical tools from other commercial manufactures which are disposable or sterilizable. The overall spatial accuracy of the integrated system can be controlled within ± 1 mm with fine tuning of the system parameters. One key functionality of the described system is its modularity in control architecture, which allows easy modification and integration of sensors and actuators if required for more complex intervention. Although in clinic, neurosurgeries quite often are more sophisticated and require sub-millimeter precision over a long duration, the methods described in this study can serve as an entry point for the further endeavor towards the real clinical application.

One limitation in the current design of the phantom is that the green tumor residues cover some tissue features, which causes small holes in the generated point-cloud of the surgical cavity and therefore may cause partial inaccuracy in the 3D model. Importantly, this limitation is not expected in the clinical setup using real brain tissue with fluorescence markers, because the vascular features of the tissue with the fluorescence contrast agents can still be detected under multimodal SFE imaging. However, the assumptions of having contiguous tumor regions that are exposed on the cavity surface must be tested *ex vivo* with follow-up pathology to determine the fluorescence target to background (T/B) thresholds required to segment the residual tumors accurately. In future work, tests with real brain tissue with fluorescently labeled tumor will be performed to verify our approach of using fluorescence T/B ratio for making a clinically relevant segmentation. We have demonstrated in [24] that mouse brain tumor can be segmented with quasi-real-time performance in the 5ALA-induced-PpIX fluorescence images taken by the SFE system. Further development of the SFE system needs to be implemented for more robust tissue imaging and ablation experiments, such as integrating optical spectroscopy during video rate imaging [25], [26]. Currently we are testing multimodal imaging of the brain tumor with “Tumor Paint” - a near-infrared fluorescence tumor indicator with very low rates of photobleaching that can be integrated with full color reflectance imaging [27], and automatic image undistortion with adaptive feed-forward control of the SFE [28].

Tissue deformation and motion is a common problem occurring during surgery and is considered to be a critical issue in medical automation. Estimation and compensation of periodic tissue motion have been studied by various research groups in beating heart surgery

[29], [30] and in image-guided radiotherapy of respiratory tumors [31]. Detection of soft tissue deformation has also been intensively studied for surgical simulation and in the laboratory using various signal modalities, such as ultrasound feedback [32], and haptic feedback [33]. Challenges still exist for real-time detection of tissue deformation and non-periodic tissue motion in the actual clinical environment, as well as the corresponding robot responses in the presence of such tissue deformation and/or motion. In the current proposed scenario, small lateral tissue motion can be compensated by the real-time endoscopic vision feedback during the robotic intervention. However, if a significant tissue motion occurs, the surgeon shall stop the current robotic intervention and either take over manually or re-initiates another robotic scan-plan-ablation routine based on his/her judgment of the scenario. And moreover, another important step towards initial in vivo testing is control of tool-tissue interaction, such as determination of safe normal and lateral tool-tissue contact forces.

Bleeding is another general risk for anyone going through a surgery. Blood obscures the surgical cavity intermittently and therefore makes the robotic intervention barely possible in this case. One possible solution would be introducing another robotic tool for blood detection and suction using the second RAVENTM II arm in left side of Fig. 2 or even manual cleaning by the surgeon in the context of shared autonomy. Such operations may slow down the main robotic intervention but will significantly increase the robustness of the surgical system overall and reduce the risk of surgery. In [34], the authors proposed algorithms based on color information and continuous blood colored regions for automatic bleeding detection in endoscopy video frames for diagnosing gastrointestinal diseases. In the future, robust and fast algorithms will need to be explored for real-time blood detection during the surgery, in which case there is a much higher volume of blood. Due to the modular design of the BT based control architecture proposed in this paper, the integration of such technology and robotic systems is considered straightforward.

Future work also includes design and implementation of an interactive graphical user interface that will visualize the ablation plan. This clinical interface will allow the surgeon to select and define regions, such as forbidden zones in the 3D model which is extremely important to preserve for the patient, and thus the robotic intervention will be prohibited inside these regions. Other features include integrating the real-time SFE videos, realistic display of the 3D model and fluorescence signal, and more operations for robot control.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Detection of mouse brain tumor cells injected with Tumor Paint (ICG dye) in near-infrared fluorescence image captured by the scanning fiber endoscope. (a) SFE image of the mouse brain tumor (blue channel: reflectance channel, green channel: fluorescence channel). (b) a closer view of the same tumor. Bright blue ring is a specular reflection of laser light entering ring of collection optical fibers in SFE.

Fig. 2.

Envision of the futuristic intelligent surgical system. The RAVENTM II surgical robot system is located on the table with right arm holding the ultra thin and flexible scanning fiber endoscope (SFE) and the surgical tool that sucks tissue fragments. The second robot arm is optional, which can be used to remove blood and manipulate the tissues. The computer monitor to the right of the robot arms depicts an SFE stereo display of the surgical cavity with manual manipulators. The smaller display on the cart to the left of the RAVENTM II depicts a single SFE view of the fluorescence-labeled tumor cavity, the tip of the suction tool with fluorescent tissue fragments, and the reflectance image of normal tissue in the background. This surgical cart represents the computer control station for directing automated residual tumor clean-up procedures with the single image-guided robot arm. Under the cart are the current power supplies and electronics for the computer and SFE. Under the table are the current electrical rack for the RAVENTM II and a futuristic fluorescence analyzer of the removed tissue fragments to determine the percentage of cells that contain the fluorescence indicator for secondary feedback.

Fig. 3.
Scanning Fiber Endoscope.

Fig. 4.
Three-Layer Control Architecture: Top layer – Behavior Tree; Middle layer - functional modules; Bottom layer - control modules.

Fig. 5. Behavior Tree representation of the semi-autonomous robotic ablation procedure. Action nodes are in green color. Logic nodes are in orange color.

Fig. 6. Dataflow pipeline for automatic image acquisition. The SFE images are published onto the network in forms of ROS Message.

Fig. 7.
Reflection removal: (a) original SFE image. (b) reflection removed in the same image.

Fig. 8.
3D reconstruction pipeline.

Fig. 9.
Feature extraction and matching between two SFE images using ORB as feature descriptor.

Fig. 10.
SFE pinhole camera model and relationship to the 3D objects.

Fig. 11.
Block diagram for tumor residue localization.

Fig. 12. Two possible cases of points p_1 and p_2 with respect to the TPS surface. (a) Case A. (b) Case B.

Fig. 13.
2D binary map of the cavity on the XY plane (white pixels represent the tumor) and contour extraction from the binary map.

Fig. 14.
Path correction using fluorescence image as feedback.

Fig. 15. 3D target projection and its correction in the segmented SFE fluorescence image. The ablation tool is 7 French ($\approx \text{Ø}2.3$ mm) in size.

Fig. 16. Path correction based on real-time SFE vision feedback. Left: Contour following, Right: Zigzag path.

Fig. 17.
Simulated surgical phantom. (a) Top view with a simulated tumor residue (green). (b)
Perspective view without tumor.

Fig. 18.

Design of the tool adapter with two setups. (a) Parallel placement design. (b) Angled placement design - front view. (c) Angled placement design - side view. (d) Robot end-effector mount with the simulated surgical phantom.

Fig. 19. Experiment setup with a RAVEN[™] II surgical robot, a SFE, a suction tool, a simulated surgical phantom and a stereo-tracker as well as a lighting system. The ablation system and the SFE control system are behind whiteboard in this photo.

Fig. 20.

The generated point-cloud and the TPS surface of the surgical cavity with the residual tumor.

Fig. 21.
Trajectories of suction tool tip (red) and SFE tip (pink) with respect to the 3D model.

Fig. 22.

3D reconstruction of the wet surface. Left: reconstructed point-cloud of the tumor and the surgical cavity without removal of specular reflections. Right: reconstructed point-cloud of the same tumor and the surgical cavity after removal of specular reflections.

Table 1

Specifications of the 3D reconstruction process

Language	C++
ROS and BT Integration	yes
Reflection Removal	yes
Feature Descriptor	ORB
Depth Recovery Order	add frame with the best triangulation
Bundle Adjustment Order	global
CPU Time (49 frames)	≈2s
Point-cloud Size (49 frames)	≈ 1000

Table 2

Execution time of each subtask

Subtask	Approx. Time in second
7x7 Raster Scanning In 4mm Spacing	196
3d Reconstruction From 49 Frames	2
Tumor Localization	3
Ablation Plan Generation	1
Robotic Ablation	136
Result Validation Via SFE Image	2

Table 3

Results for 10 trial runs

Trial #	Number Of Tumor Residues	Path Pattern	Result	Fail Reason
1	1	zigzag	success	
2	1	contour parallel	success	
3	1	mix	success	
4	1	mix	fail	residue remained partially uncleaned
5	1	contour parallel	success	
6	2	contour parallel /small	success	
7	2	mix / small	fail	smaller residue remained uncleaned
8	2	mix / mix	success	
9	2	contour parallel /mix	fail	tool tip bumped into the surgical phantom
10	2	contour parallel /zigzag	success	