Microscope-integrated optical coherence tomography for in vivo human brain tumor detection with artificial intelligence

Patrick Kuppler, MD,1 Paul Strenge,2 Birgit Lange, PhD,2 Sonja Spahr-Hess,1 Wolfgang Draxinger,3 Christian Hagel, MD,4 Dirk Theisen-Kunde,2 Ralf Brinkmann, PhD,2,3 Robert Huber, PhD,3 Volker Tronnier, MD,1 and Matteo Mario Bonsanto, MD1

1Department of Neurosurgery, University Medical Center Schleswig-Holstein, Campus Luebeck; 2Medical Laser Center Luebeck; 3University of Luebeck, Institute of Biomedical Optics, Luebeck; and 4University Medical Center Hamburg-Eppendorf, Institute of Neuropathology, Hamburg, Germany

OBJECTIVE It has been shown that optical coherence tomography (OCT) can identify brain tumor tissue and potentially be used for intraoperative margin diagnostics. However, there is limited evidence on its use in human in vivo settings, particularly in terms of its applicability and accuracy of residual brain tumor detection (RTD). For this reason, a microscope-integrated OCT system was examined to determine in vivo feasibility of RTD after resection with automated scan analysis.

METHODS Healthy and diseased brain was 3D scanned at the resection edge in 18 brain tumor patients and investigated for its informative value in regard to intraoperative tissue classification. Biopsies were taken at these locations and labeled by a neuropathologist for further analysis as ground truth. Optical OCT properties were obtained, compared, and used for separation with machine learning. In addition, two artificial intelligence–assisted methods were utilized for scan classification, and all approaches were examined for RTD accuracy and compared to standard techniques.

RESULTS In vivo OCT tissue scanning was feasible and easily integrable into the surgical workflow. Measured backscattered light signal intensity, signal attenuation, and signal homogeneity were significantly distinctive in the comparison of scanned white matter to increasing levels of scanned tumor infiltration (p < 0.001) and achieved high values of accuracy (85%) for the detection of diseased brain in the tumor margin with support vector machine separation. A neuronal network approach achieved 82% accuracy and an autoencoder approach 85% accuracy in the detection of diseased brain in the tumor margin. Differentiating cortical gray matter from tumor tissue was not technically feasible in vivo.

CONCLUSIONS In vivo OCT scanning of the human brain has been shown to contain significant value for intraoperative RTD, supporting what has previously been discussed for ex vivo OCT brain tumor scanning, with the perspective of complementing current intraoperative methods for this purpose, especially when deciding to withdraw from further resection toward the end of the surgery.

https://thejns.org/doi/abs/10.3171/2024.1.JNS231511

KEYWORDS optical coherence tomography; brain tumor imaging; residual tumor detection; tumor border detection; tissue classification; in vivo imaging; artificial intelligence; automated tissue characterization; oncology

Abbreviations: AI = artificial intelligence; CLE = confocal laser endomicroscopy; EOR = extent of tissue resection; EPMR = early postoperative magnetic resonance; FNa = fluorescein sodium; OCT = optical coherence tomography; RTD = residual brain tumor detection; SVM = support vector machine; 5-ALA = 5-aminolevulinic acid.

Submitter: Patrick Kuppler; Accepted: January 30, 2024.

Include when citing: Published online May 3, 2024; DOI: 10.3171/2024.1.JNS231511.

© 2024 The authors, CC BY-NC-ND 4.0 (http://creativecommons.org/licenses/by-nc-nd/4.0/)
components, and subsequently captured by a receiver. The resulting image impressions are comparable to those of ultrasound images, where the flight time difference between acoustic waves within a tissue is measured. However, unlike ultrasound, OCT achieves near microscopic resolution. Studies with ex vivo experiments have demonstrated that OCT imaging exhibits high levels of accuracy in detecting brain tumor tissue, with sensitivity and specificity values ranging from 90% to 100% and from 76% to 96%, respectively.1–4 However, there is limited evidence of in vivo application, where integration into a surgical setting is technically complicated and involves many hurdles, which is why research mostly concentrates on ex vivo tissue scanning. Therefore, the complete potential of this technology has yet to be fully demonstrated. In 2007, Haag-Streit launched commercial sales for the SD OCT System that was integrated into a standard microscope, allowing the user to scan underlying tissue without the need for further equipment during microsurgical procedures.

In an attempt to evaluate this technology for in vivo application with regard to residual brain tumor detection (RTD), 3D tissue scans were executed at the resection margin of 18 brain tumor patients and tissue biopsies were acquired for histopathological correlation. The accuracy of RTD through automated OCT scan analysis was then compared to techniques that are commonly used in clinical practice for this purpose.

**Methods**

**Surgical Procedure With Fluorescein and Neuronavigational Guidance**

The inclusion criteria for the study were patients (age > 18 years) with supratentorial brain tumors and suspected brain malignancies outside of eloquent cortex. Informed written consent was obtained from a total of 21 patients prior to the procedure. Approval was granted by the ethics committee of the University of Lübeck. All procedures were performed according to clinical standards.

For intraoperative fluorescence guidance, all patients received 4 mg/kg body weight of fluorescein (Alcon, 10% at 100 mg/ml; registration no. 6375757.00.00) intravenously after induction of general anesthesia and before opening the dura mater. Tumor resection was carried out 15 minutes after the injection of fluorescein sodium (FNa). The excitation wavelength was 460–500 nm, and the cut-off wavelength was 510 nm (refer to Fig. 1C). BrainLab VectorVision and its neuronavigation feature were used to confirm extent of tissue resection (EOR). Subsequent documentation included whether total or subtotal resection was achieved. If neuropathological analysis found tumor infiltration in any of the acquired biopsies, while total resection was surgically assumed, that patient was classified as false negative on the basis of FNa diagnostics. The analysis included all 21 participating patients.
Microscope-Integrated OCT Scanning

The Haag-Streit (HS Hi-R NEO 900) microscope (refer to Fig. 1B) was used for the microsurgical approach. The integrated SD OCT System by Haag-Streit (OptMedt iOCT) was used for tissue scanning after visually identifying tissue at question in the resection cavity. The iOCT functions at a central imaging wavelength of 830 nm and an A-scan rate of 35,000/sec, accomplishing axial and lateral resolution of 8 μm (in air) and 23 μm (in air), respectively. To acquire a 90° angle from the light source to the tissue, the microscope arm was manually shifted. High resolution with adequate relative backscattered signal intensity was attained by setting the working distance to 300 mm at zoom level 9 for all scans. The field of vision was confined to a frame measuring 5.7 × 15.7 mm, as previously described. The signal was measured to tissue depths as far as 1 mm. After tumor removal, 5 predetermined sites in the resection cavity were scanned to ensure comprehensive coverage of the entire resection zone. Each scanning process took approximately 30 seconds.

In total, 108 volume scans from 21 patients were initially captured for this study. Full datasets of 3 patients (1 with glioblastoma and 2 with adenocarcinoma metastasis) and a total of 64 volume scans had to be excluded due to empty information or scan artifacts, such as signal fold-over. Ultimately, 44 OCT volume scans of in vivo brain and brain tumor were finally used for further OCT scan analysis.

Biopsies and Histology

MRI-guided tissue biopsies were obtained for histopathological correlation at designated locations after OCT scanning (refer to Fig. 1A and B). The average tissue sample size measured 4 × 4 × 2 mm. Each tissue sample underwent histological preparation and was analyzed by an experienced neuropathologist (C.H.) to validate tissue type and residual tumor burden. Each specimen was stained using hematoxylin and eosin and segmented through the assistance of a tissue-labeling system. Labels identify white matter, edematous tissue, gray matter, or varying degrees of tumorous infiltration (low, 0%–30% tumor infiltration; medium, 30%–60% tumor infiltration; high, > 60% tumor infiltration). The prevalence of the primary tumor types is presented in Table 1, while Fig. 2 shows histopathological samples.

Early Postoperative MRI

Within 72 hours after surgery, each patient underwent 3D gadolinium MRI at a dose of 0.2 mg/kg body weight for detection of tumor residues. The results were later compared to histopathological findings to verify the accuracy of RTD. If histopathological findings showed residual tumor and MRI did not demonstrate tissue enhancement, then that particular MRI scan was considered false negative. All 21 participating patients were considered for analysis.

Scan Analysis

En face OCT images were generated from the original OCT volumes through the use of custom-written code (MATLAB 9.10.0 R2021a, The MathWorks, Inc.). Refer to Fig. 1D for the images and Fig. 1E for the original volumes.

TABLE 1. List of the tumor entities of 18 brain tumor patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>002</td>
<td>Anaplastic oligodendroglioma (WHO grade III)</td>
</tr>
<tr>
<td>003</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>004</td>
<td>Metastasis (lymphoma)</td>
</tr>
<tr>
<td>005</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>006</td>
<td>Neuroendocrine carcinoma (WHO grade III)</td>
</tr>
<tr>
<td>007</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>008</td>
<td>Anaplastic astrocytoma (WHO grade III)</td>
</tr>
<tr>
<td>009</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>010</td>
<td>Metastasis (renal cell carcinoma)</td>
</tr>
<tr>
<td>011</td>
<td>Metastasis (adenocarcinoma)</td>
</tr>
<tr>
<td>012</td>
<td>Anaplastic oligodendroglioma (WHO grade III)</td>
</tr>
<tr>
<td>013</td>
<td>Metastasis (ovarian cancer)</td>
</tr>
<tr>
<td>014</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>015</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>016</td>
<td>Metastasis (melanoma)</td>
</tr>
<tr>
<td>017</td>
<td>Anaplastic oligodendroglioma (WHO grade III)</td>
</tr>
<tr>
<td>018</td>
<td>Glioblastoma</td>
</tr>
</tbody>
</table>

Only OCT signaling from the area of biopsy acquisition (region of interest) was used for histopathological correlation. For visual assessment of each OCT volume, we performed surface normalization and applied a Jet color map array with varying backscattered signal intensity values ranging from 40 to 70 dB using open-source software (ImageJ, version 1.53a, National Institutes of Health) (refer to Fig. 1F).

For retrospective scan analysis, patches were manually segmented from OCT B-scans. These patches exclusively consist of valid OCT data and are free from artifacts and empty information. A total of 914 patches of size 144 × 56 pixels were extracted (refer to Fig. 3B). The distribution of these B-scan patches across the tissue labels is presented in Fig. 3C.

Tumor Classification Using Machine Learning With Optical Values

Optical value determination is a key component of OCT scan analysis that enables the extraction of necessary data from the scans. The signal obtained comprises information from the medium illuminated by the incident light. \( I \) represents the intensity of the backscattered signal detected by the OCT system, while \( \mu \) is the attenuation coefficient that characterizes the signal’s depth-wise decay. A-scan variability within a B-scan was termed \( r^2 \) for assessing structural uniformity, whereas \( I \) and \( \mu \) correspond to the optical properties of the tissue. For statistical analysis, we evaluated the respective mean values for normal distribution using the Shapiro-Wilk test. We performed pairwise comparisons of these values using the Wilcoxon signed-rank test. In terms of classification based on optical properties, a support vector machine (SVM) with a linear kernel was utilized.

Tumor Classification Using Artificial Intelligence

Two distinct techniques were implemented to classify...
FIG. 2. Examples of hematoxylin and eosin–stained tissue samples of white matter (A), 0%–30% tumor infiltration (i.e., low infiltration) (B), 30%–60% tumor infiltration (medium) (C), > 60% tumor infiltration (high) (D), gray matter (E), and edematous white matter (F). Image size 300 µm × 300 µm. Figure is available in color online only.

FIG. 3. Surface-normalized and color-mapped B-scan (the Jet array displays backscattered signal intensity I in decibels) (A), extracted B-scan patches from OCT volumes (red rectangles) (B), and bar chart with the distribution of B-scan patches with regard to the tissue label (GM0% = gray matter; WM0% = white matter; WM0–30% = low tumor infiltration; WM30–60% = medium tumor infiltration; WM > 60% = high tumor infiltration; WME = edematous white matter) (C). The various colors in the bar graph indicate respective patients. Figure is available in color online only.
OCT B-scan patches. The initial method utilized a convolutional neural network to distinguish healthy tissue from pathological brain tissue. The second approach involved an autoencoder network to extract unsupervised features. The encoder’s output was subsequently used to train a fully connected neural network. Artificial intelligence (AI) training entailed a leave-one-out approach. For each training configuration, we used 1 patient for the test data while the remaining patients were designated for training. Specificity, sensitivity, and balanced accuracy were obtained using the mean sensitivity and specificity of all training folds. The overall performance of the approach was evaluated. Refer to Fig. 4 for an overview of the AI architecture.

Results

OCT Scan Analysis

Tumor Classification Using Machine Learning With Optical Values

The data demonstrated a significant discrepancy in the comparison of optical values based on their histopathological classification. In pairwise comparison between white matter and low, medium, and high tumor-infiltrated tissue in all optical values, p values < 0.001 were achieved. Figure 2C–E displays these findings, where all values decrease with increasing grade of tumor infiltration. The measured values for white matter indicated it to be smooth and homogenous with high scattering properties, which is why the attenuation and backscattered intensity are high. Tumor-infiltrated tissue had the opposite values. Gray matter showed similar optical values to the tumor-infiltrated tissue, which is why there is no statistical difference in attenuation or homogeneity and why only in comparison to low and medium tumor-infiltrated tissue are there significant differences with p < 0.01 when assessing signal intensity. The $r^2$ value suggests a tissue structure with lower scattering properties and more heterogeneity. Edematous tissue demonstrates a more homogeneous structure compared to tumor infiltration but is still more heterogeneous than healthy white matter. In terms of attenuation and backscattered signal intensity, edema is more similar to tumor infiltration than white matter, exhibiting high light absorption with low backscattering intensity and retaining homogeneity throughout the scan. Figure 5A and B illustrates relationships between optical values. The measured similarity of values for gray matter and various tumor infiltration grades created a significant cluster. Values measured for edematous tissue and white matter formed a separate cluster. To evaluate tumor detection accuracy based on these image value clusters, an SVM was utilized in a combined approach to establish binary linear classifications for sensitivity and specificity calculations. Two classification tasks were defined for the study. Task I utilized all available data for the classification, with gray and white matter assigned to the nonpathological class and the remaining tissue labels assigned to the pathological class. Task II specifically focused on separating white matter from tumor infiltration. Sensitivity, specificity, and balanced accuracy values for each task are presented in Table 2. The combined SVM approach data demonstrated high accuracy (85%) for the separation of white matter from all degrees of tumor infiltration (task II). However, incorporating gray matter and edematous tissue into the nonpathological class resulted in decreased accuracy (57%) in that separation task (task I).

Tumor Classification Using AI

The results demonstrated that both AI approaches

FIG. 4. Overview of the architectures used for the different classification approaches. The architecture of convolutional neural network A and of the autoencoder combined with the fully connected layers for classification B are shown. Figure is available in color online only.
performed well in classifying white matter with different grades of tumor infiltration. However, both struggled to accurately classify healthy tissue from pathological tissue when gray matter was included (task I). Overall, the autoencoder network approach exhibited superior performance compared to the convolutional neural network approach and achieved a similar performance to the SVM approach (refer to Table 2).

**Fluorescence Guidance**

In 16 patients, total tumor resection was anticipated through assessment of the absence of fluorescence signaling and consulting neuronavigation. Suspected residual tumor was documented in the remaining 5 patients. Only in 9 cases, however, were all tissue biopsies labeled free of tumor infiltration. If subtotal resection was expected (5 patients), histopathological findings confirmed legitimate residual tumor. When fluorescence guidance was assessed and neuronavigation consulted, only 67% of the anticipated outcomes were accurately reflected by the histopathological findings, resulting in a sensitivity of only 42%.

**Early Postoperative MRI**

In 12 patients, neuroradiology did not register gadoxilium enhancement in the early postoperative magnetic resonance (EPMR) imaging, while free margins were con-

---

**TABLE 2. Sensitivity, specificity, and balanced accuracy of both CNN and AE classification approaches and combined optical parameters with SVM separation for specific classification tasks**

<table>
<thead>
<tr>
<th>Classification Approach</th>
<th>Task I*</th>
<th>Task II†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
<td>Specificity (%)</td>
</tr>
<tr>
<td>CNN</td>
<td>59</td>
<td>77</td>
</tr>
<tr>
<td>AE</td>
<td>65</td>
<td>66</td>
</tr>
<tr>
<td>Optical values w/ SVM</td>
<td>98</td>
<td>16</td>
</tr>
</tbody>
</table>

AE = autoencoder network; CNN = convoluted neural network.
* Task I included full data.
† Task II included classification of tumor infiltration in white matter.
confirmed in only 9 patients through tissue biopsies. Three patients, all of whom had glioblastoma, were falsely determined to be tumor free by neuroradiology. In the remaining 9 patients, in whom EPMR imaging showed signs of tumor residues, histopathological analysis confirmed residual tumor. The estimated EPMR-based sensitivity in this study for the detection of residual tumor was 75%.

Discussion

Tumor resection is an essential component of neuro-oncological treatment protocols, and maximal EOR has proven to be advantageous for overall and disease-free survival. Total removal of a tumor relies heavily on a surgeon’s expertise and the application of perioperative diagnostics that help distinguish between tumorous and healthy brain tissue. A variety of techniques and technologies are currently available for this purpose, all with intrinsic advantages and disadvantages.

Fluorescence-guided surgery with fluorophores, such as 5-aminolevulinic acid (5-ALA) or FNa, has been shown to increase EOR and subsequently progression-free survival in glioma patients. 5-ALA is selectively taken up and metabolized by malignant glioma cells, whereas FNa accumulates in regions of the brain where the blood-brain barrier has been compromised. Photosensitivity reactions are recognized adverse events of 5-ALA. Also, administration must be induced orally 4 hours prior to surgery, which is more inconvenient for the patient compared to FNa, for which administration can be induced shortly before tumor resection and the reported adverse effects are rare. In a prospective phase II study conducted across multiple centers (FLUOGLOI), Acherbi et al. reported sensitivity and specificity values of 80.8% and 79.1%, respectively, for FNa guidance in identifying tumor tissue. Here, tissue biopsies were obtained specifically from fluorescent and nonfluorescent tissue and later analyzed for accuracy of tumor detection. In this study, however, evaluation of the accuracy of FNa-guided surgery was performed by taking navigated biopsies from different distant areas within the borders of the resection cavity (frontal, medial, lateral, occipital) after complete resection of the tumor had been documented according to the study protocol. The aim was to assess histopathological information on the overall radi- cality of the EOR itself by taking representative biopsies from the entire resection cavity, particularly after surgical trauma possibly affected the blood-brain barrier in adjacent healthy tissue and FNa penetration was already decreasing at the end of the surgery, thereby resulting in less specific fluorescence signaling. This may be the reason why in this study a combined sensitivity for FNa guidance and confirmation with neuronavigation of only 42% was obtained. Although only identified in a small cohort of 21 patients, these findings indicate that current techniques for intraoperative RTD are far from reliably accurate, particularly for determining the appropriate time to forgo further tissue resection at the end of the surgery. These findings demonstrate the difficulty of identifying the correct tumor margin and achieving complete tumor removal.

On the same note, only 75% sensitivity for EPMR imaging was found in this work when histopathological find-ings were compared to gadolinium enhancement. Though having proved to be valuable for assessing EOR in multiple studies, accuracy of EPMR imaging for RTD in this study suggests a more realistic assumption of having achieved complete tumor removal from the operating site. In this regard, Li et al. observed that supramarginal resec- tion beyond the T1-weighted contrast-enhanced glioblas-toma and > 50% of the FLAIR abnormality region was associated with prolongation of overall survival, presumably due to further tumor removal that was not detected through gadolinium enhancement. The use of intraoperative MRI has shown promising potential for RTD, where Heßelmann et al. reported 95% sensitivity and 69.5% specificity when assessing multiple MRI sequences after first resection and correlation of histopathological findings after a second round of resection, when residual tumor was detected with beneficial impact on overall and progression-free survival. However, intraoperative MRI presents economic challenges for any department, necessitates specific operating room conditions, and has been shown to significantly prolong operative time when compared to traditional operating rooms, which is why this technique is not standard of care in brain tumor surgery today.

Improving intraoperative RTD is therefore a pivotal component of neurosurgical research. Various laser-based imaging techniques, such as CLE, Raman spectroscopy, or multiphoton laser microscopy, are advancing to provide real-time histopathologic information during tumor resec- tion. The detection of intraoperative brain tumors has ex- hibited favorable outcomes in several study designs, with variable sensitivity and specificity values lying between 90% and 96% and between 94% and 100%, respectively. However, all these modalities share limitations of requiring either tissue removal from the surgical site for ex vivo application or the need for a contact-based imaging probe in vivo, which is not required in the technology demonstrated in this study, where the neurosurgical workflow, with the operation under the microscope, is not disturbed. In the example of CLE, fluorescent light reflection is used for obtaining in vivo optical biopsies of tissue in the tumor margin with a handheld probe in a contact-based manner. These biopsies are examined simultaneously by a neuro-pathologist, specifically trained in interpreting CLE images, at a cloud-based workstation located remotely.

OCT, on the other hand, has the ability to provide noncontact in vivo applications without requiring extra imaging equipment. It also presents the opportunity for automated tissue classification in real time. Research on neurosurgical in vivo application, however, is still mostly focused on feasibility. In this microscope-integrated approach, it was demonstrated for the first time that high RTD values could be achieved in vivo with automated im-age feature recognition, supporting what has well been des- cribed for ex vivo OCT brain tumor scanning. However, on-sight scan analysis was not yet feasible in this study. Without further image processing, analysis of signal measurements, or automated image classification, this OCT system cannot be used for intraoperative RTD.

Retrospective assessment of differences in optical val- ues (I, µ, r²) and use of them for separation in a combined SVM approach achieved an accuracy of 85%. Highly sig-
significant differences in all three image values were found when comparing tissue labels, especially between healthy white matter and different degrees of tumor-infiltrated tissue with p values far below a set limit value of 0.05. Yashin et al. explained high light attenuation of healthy white matter with the presence of highly scattering myelin fibers, which for the most part are not present in healthy gray matter. In theory, a higher degree of tumor infiltration would then result in a higher degradation of myelin fiber, consequently leading to a decrease of light attenuation.

Classification based on neural networks and autoencoder augmentation achieved accuracy values of 82% and 85%, respectively, when distinguishing between white matter and tumor infiltration. Juarez-Chambi et al. achieved sensitivity of 99% and specificity of 86% with an AI-assisted A-scan–based approach. The data consisted of ex vivo OCT A-scans acquired by an OCT system with a lateral resolution of 16 µm and an axial resolution of 6.4 µm. Scans were taken from fresh tissue biopsies that were acquired from the main tumor and from the resection margin. Unlike other research groups, however, the work presented here focuses on differentiating tissue at the resection margin, where tissue with different degrees of tumor infiltration could be assessed. Comparison to other groups is therefore complicated, given that most do not differentiate between various stages of tumor infiltration in as much detail as this work did. In addition, executing OCT scanning in vivo—where conditions are more complicated due to the pulsatile brain movement, containment of the resection cavity, and lack of space for additional instruments—is a more complex undertaking. Therefore, integrating such a system into a surgical microscope appears to be a way of overcoming the latter obstacle.

One major challenge remains: optimal manual adjustment of the microscope for exploring the resection cavity. The accessibility of the cavity can be inconvenient due to its varying dimensions. Focusing at a 90° angle on the surface of the tissue was particularly difficult. The integration of a robotic system that would automatically traverse resection cavities would simplify this step. Technical developments in this area are on the rise and have been well demonstrated experimentally. This, combined with a lack of intraoperative scan quality validation, led to a large number of scans with artifacts that had to be excluded from further analysis. Only 44 volume scans from 18 patients were included in the final analysis, whereas 108 volume scans from 21 patients were initially captured for this study, resulting in 60% dropout of the gathered data. This is why the overall applicability of this microscope-integrated technology shows need for improvement while reaching its limits in extreme angles.

The presented results from the remaining eligible scans, however, have shown that high RTD values in vivo are achievable and comparable to what has been described for 5-ALA–guided surgery, for which mean sensitivity and specificity in distinguishing tumor from healthy brain tissue at the resection edge ranged between 83% and 87% and between 89% and 91%, respectively, in multiple meta-analyses, and are superior in accuracy to FNa guidance in both the literature and this work. The accuracy of RTD is even superior to what can be found for EPMR imaging in this study and comparable to what can be found in the literature. Interestingly, this in vivo approach holds up with the results achieved on ex vivo OCT scan analysis, where implementation is much less complex.

For edematous tissue, Rodriguez et al. reported that edema in the gray matter of mice can reduce the attenuation coefficient by as much as 8%. In this work, the attenuation coefficient of edema in white matter was around 40% lower than in healthy white matter while showing significant lower backscatter intensity; these findings combined indicate an absorbing characteristic of edema. Distinction between healthy and edematous tissue is therefore feasible in vivo when assessing optical value analysis.

This work found that gray matter produced OCT scans similar to those of tumor-infiltrated tissue, which explains the insufficient results obtained in task I and poses a significant limitation of this technology. However, whether differentiation of gray matter in comparison to tumor tissue is critical for evaluation of this technology is debatable, as its strength lies in detecting tumor residues in the resection cavity toward the end of the surgery, where the distinction from white matter is much more essential.

Conclusions

In vivo OCT scan analysis of the resection cavity has proven to contain additional information on residual tumor after brain tumor surgery, supporting what has well been described for ex vivo OCT brain tumor scanning. More than half of the scans did not seem to be fit for further analysis, which for the most part was caused by a missing validation of intraoperative scan quality. In the remaining scans, in vivo OCT scanning provided higher accuracy values in RTD when compared to FNa guidance or EPMR imaging in this study. OCT technology integrated into a surgical microscope is a system in evolution. With further development in user-friendly applications and integration of real-time tissue analysis, this system has high potential for future intraoperative use for RTD. Applying AI for image feature recognition has shown promising results and may be crucial to achieve high accuracy in RTD, with the prospect of complementing current intraoperative methods, particularly when deciding on withdrawing from further resection at the end of brain tumor surgery. Whether OCT-based resection will then have an impact on overall and progression-free survival, however, is subject to future observation.

Acknowledgments

This research was funded by the Federal Ministry of Education and research grants nos. 13GW0227A, 13GW0227B, and 13GW0227C; the European Union Project ENCOMOLE-2i (Horizon 2020, ERC CoGino, 646669); the state of Schleswig-Holstein (Excellence Chair Programme); and Deutsche Forschungsgemeinschaft (EXC 2167-39084018).

References


Disclosures

Dr. Huber reported shares from Optores GmbH and royalties from LMU Munich and the University of Lübeck during the conduct of the study; shares from Optores outside the submitted work; a patent for US 7414779 B2 with royalties paid from Abbott; a patent for DE 10 2018 212 100 B2 with royalties paid from Optores; a patent for US 8855149 B2 with royalties paid from Optores; and a patent for EP 2557441 B1 with royalties paid from Optores.

Author Contributions

Conception and design: Kuppler, Streng, Brinkmann, Huber, Bonsanto. Acquisition of data: Kuppler, Streng, Lange, Spahr-Hess, Draxinger, Hagel. Analysis and interpretation of data: Kuppler, Streng, Bonsanto. Drafting the article: Kuppler. Critically revising the article: Streng, Theisen-Kunde, Brinkmann, Huber, Tromnier, Bonsanto. Reviewed submitted version of manuscript: Kuppler, Bonsanto. Proposed the final version of the manuscript on behalf of all authors: Kuppler. Statistical analysis: Kuppler, Streng. Administrative/technical/material support: Kuppler, Streng, Lange, Theisen-Kunde, Brinkmann, Huber, Tromnier, Bonsanto. Study supervision: Kuppler, Bonsanto.

Correspondence

Patrick Kuppler: University Medical Center Schleswig-Holstein, Campus Luebeck, Germany, patrick.kuppler@uksh.de.


