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Open access segmentations of intra-operative brain tumor ultrasound images

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Abstract

Purpose: Registration and segmentation of magnetic resonance (MR) and ultrasound (US) images could play an essential role in surgical planning and resectioning brain tumors. However, validating these techniques is challenging due to the scarcity of publicly accessible sources with high-quality ground truth information. To this end, we propose a unique set of segmentations (RESECT-SEG) of cerebral structures from the previously published RESECT dataset to encourage a more rigorous development and assessment of image processing techniques for neurosurgery.

Acquisition and Validation Methods: The RESECT database consists of MR and intra-operative US (iUS) images of 23 patients who underwent brain tumor resection surgeries. The proposed RESECT-SEG dataset contains segmentations of tumor tissues, *sulci*, *falk cerebri*, and resection cavity of the RESECT iUS images. Two highly experienced neurosurgeons validated the quality of the segmentations.

Data Format and Usage Notes: Segmentations are provided in 3D NIFTI format in the OSF open-science platform: <https://osf.io/jv8bk>.

Potential Applications: The proposed RESECT-SEG dataset includes segmentations of real-world clinical US brain images that could be used to develop and evaluate segmentation and registration methods. Eventually, this dataset could further improve the quality of image guidance in neurosurgery.

42 I. Introduction

43 Gliomas are the most common malignant primary brain tumors originating from glial cells
44 and are classified into grades 1-4 by the World Health Organization (WHO)^{1,2}. Grades 1-
45 2 are low-grade, while grades 3-4 are high-grade tumors³. Surgical resection is a standard
46 treatment for gliomas, and pre-operative magnetic resonance (MR) imaging is used for tumor
47 characterization. However, brain tissue deforms during surgery due to factors like edema and
48 gravity (i.e. brain shift)⁴, rendering pre-operative MR images inaccurate. Acquiring data at
49 different stages during surgery helps the surgeon better monitor the progress of the tumor
50 resection and, consequently, operate more precisely. Intra-operative imaging, particularly
51 intra-operative MR (iMR) and intra-operative ultrasound (iUS) aids surgeons by providing
52 updated guidance^{5,6,7}. While iMR offers superior image quality, it is costly, adds a long
53 time to the operation, and requires dedicated operating rooms^{8,9}. In contrast, iUS is a cost-
54 effective, flexible, and versatile modality that presents real-time scanning without altering
55 the surgical workflow^{10,11,12}. Due to the easy procedure of acquiring iUS rather than iMR,
56 several recent studies have demonstrated the use and interest in iUS in neurosurgery^{8,11,12,13}.

57 While iUS presents several advantages in the context of brain tumor resection, ultra-
58 sound (US) images can be difficult to interpret. Non-standard imaging planes and unfamiliar
59 contrast are major factors limiting the efficient and widespread use of US in neurosurgery.
60 To mitigate such limitations and fully leverage the advantages of iUS, automated image seg-
61 mentation of structures such as tumors within iUS images can provide valuable assistance to
62 neurosurgeons during procedures. Recent automated image segmentation algorithms, such
63 as deep learning (DL) algorithms have made advancements in brain tumor segmentation
64 from both US^{14,15,16,17} and MR^{18,19,20,21} images. However, access to high-quality datasets ex-
65 pertly annotated is essential for the development and validation of DL algorithms²². In the
66 context of medical imaging, MR images have seen more readily available datasets compared
67 to other modalities, making them the primary focus for DL algorithm development. The
68 BRATS challenge, among others, stands out as a prominent dataset with valuable annota-
69 tions that have significantly contributed to the evolution and refinement of DL algorithms²³.
70 Acquiring such data, especially for iUS images, is expensive and rare.

71 Currently, there are only three publicly available datasets that provide iUS brain im-
72 ages, the BITE dataset²⁴, the RESECT database²⁵, and ReMIND²⁶. The BITE dataset
73 contains pre- and post-operative MR scans as well as multiple iUS images of 14 patients.
74 The RESECT database contains pre-operative MR scans and iUS images from 23 patients
75 with low-grade gliomas. The ReMIND dataset contains 369 pre-operative MR scans, 320 3D
76 iUS scans, 301 iMR scans, and 356 pre-operative MR segmentations of 114 patients. None of
77 the abovementioned datasets contain segmentation of anatomical structures in the iUS im-
78 ages, thereby hindering the development and validation of iUS processing methods. For the
79 RESECT database, a few research groups have previously conducted segmentations of iUS
80 images^{14,18,27}. However, a portion of these annotations remained inaccessible to the public,
81 and in some instances, only a small subset of cases was segmented, with limited validation
82 procedures in place.

83 In this work, we present the most comprehensive and validated expert segmentations of
84 cerebral structures in iUS images from the RESECT database. The focus of the RESECT-
85 SEG dataset is on delineating the tumor in pre-resection iUS 3D volumes and identifying the
86 resection cavity during and after the surgery. To enhance the surgeon’s ability to achieve
87 more precise tumor resection, *sulci* and the *falx cerebri*, whenever they were within the
88 field of view, were also delineated. These structures commonly serve as crucial anatomical
89 references for surgeons, given their clear visibility in iUS images. The following sections
90 detail the segmentation and validation protocols for all the mentioned structures in the iUS
91 images and brain tumor segmentation in pre-operative MR images.

92 II. Acquisition and Validation Methods

93 In this section, a comprehensive overview of the dataset is presented, along with detailed an-
94 notations for various anatomical structures, including tumors, resection cavities, *falx cerebri*,
95 and *sulci*. The annotation process involved the utilization of two primary tools: ITK-SNAP²⁸
96 and 3D Slicer²⁹, chosen based on individual preference and familiarity. Furthermore, specific
97 built-in features of these software platforms were leveraged as necessary, such as smoothing
98 and interpolation functionalities, to enhance the accuracy and completeness of the annota-
99 tions. Further elaboration on these tools and their respective functionalities is provided in
100 the subsequent paragraphs. Given that both ITK-SNAP and 3D Slicer are widely used tools
101 in the field, the decision to select one over the other was solely based on our inter-group
102 preferences. It is important to highlight that manual segmentation entails human judgment
103 and expertise, enabling nuanced interpretation and adjustments tailored to the anatomical
104 complexities of each case. Consequently, the choice of segmentation software or algorithm
105 does not introduce bias, as it depends on the proficiency and diligence of the annotators.

106 II.A. RESECT Database

107 The RESECT database²⁵ comprises pre-operative contrast-enhanced T1-weighted and T2
108 FLAIR MR scans alongside three 3D volumes of iUS scans from 23 patients with low-grade
109 gliomas (grade 2) who underwent surgeries between 2011 and 2016 at St. Olavs University
110 Hospital, Trondheim, Norway. The iUS scans were acquired at three different stages of
111 the procedure: before resection, during resection, and after resection for control. These US
112 images were captured by an expert surgeon, and the database includes manual neuroanatomy
113 landmarks, facilitating MR-to-US volume registration and inter-US volume alignment. The
114 details of the image acquisition procedure can be summarized as follows:

- 115 • Pre-operative MR scans: T1-weighted and T2 FLAIR sequences were acquired on 3T
116 Magnetom Skyra MR scanners, both with 1 mm isotropic voxel size, except three
117 patients who underwent the MR imaging on a 1.5T Magnetom Avanto MR scanner
118 with 1 mm slice thickness.

- Intra-operative US scans: 3D US images collected using a 12FLA-L linear probe of Sonowand Invite neuronavigation system with a frequency range of 6-12 MHz integrated with the NDI Polaris optical tracking system.

122 II.B. iUS Tumor Segmentation Protocol

123 Tumoral tissue in US images is typically identified through abnormal echogenicity or texture variations compared to healthy tissue. Echogenicity refers to the level of reflectivity or brightness of tissue on a US image. In this context, variations in echogenicity indicate potential areas of malignancy, allowing medical professionals to identify and examine potential cancerous lesions. In the study, 19 out of 23 cases' iUS images (cases 1 to 23) were segmented, initially following Munkvold et al.'s method²⁷. In these cases, initial US volume segmentations were already available. Four cases (cases 24 to 27) without prior iUS segmentations relied on MR segmentations to define the tumor region of interest in iUS images. To be more specific, for these four cases, the MR segmentation served as a starting point to define the region of interest (ROI) for the tumor in the iUS images. Further details of the MR segmentation protocol can be found in the work of Munkvold et al.²⁷.

134 In the iUS segmentation protocol, 3D Slicer²⁹, a free and open-source medical image analysis software, was employed to perform ground truth segmentations on the acquired iUS images. For cases 24 to 27 that were initiated with MR segmentations due to brain shift during resection surgery, the boundaries of the tumor in the US images and MR tumor segmentations did not align²⁵. This discrepancy necessitated the registration of MR tumor segmentations to iUS images using available landmarks from the RESECT database. This registration process effectively mitigated the misalignment of tumor borders between the iUS images and their corresponding MR tumor segmentations. Therefore, for cases 24 to 27, the MR segmentations were imported into the 3D Slicer scene and after the registration step, they were utilized as the initial delineation for iUS.

144 In all cases, to refine the initial 3D US tumor segmentations, the Label Map Smoothing module, an existing feature in 3D Slicer, was employed. Subsequently, the smoothed tumor segmentations were manually fine-tuned to ensure accurate coverage of the tumor region in the iUS image. To facilitate further correction, FLAIR MR images were registered to iUS images since MR images were unaffected by brain-shift effects. These complementary overlays served as guidance for generating more precise iUS tumor segmentations. An illustrative example of tumor segmentation is provided in Fig. 3 (a)-(d).

151 II.C. iUS Resection Cavity Segmentation Protocol

152 Resection cavity segmentation in iUS images encompasses the volume where tissue has been resected or retracted during image acquisition. Resection, a surgical procedure characterized by the complete removal of tissue or tumors, contributes to the formation of a distinct three-dimensional space within the brain known as the resection cavity. On the other hand, retraction, another surgical maneuver, entails cutting tissue and displacing it to the side

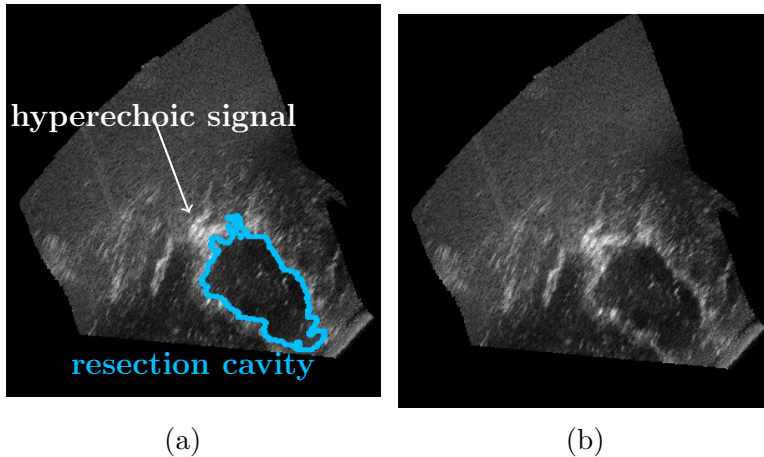


Figure 1: Ultrasound image of a resection cavity (a) with and (b) without segmentation.

157 without complete removal. Hyperechoic signals surrounding cavities in iUS images result
 158 from sound attenuation differences between brain tissue and saline water, as well as the
 159 presence of blood (see Fig. 1)³⁰. To prevent false positives, only homogeneous, dark signals
 160 were considered as cavities, potentially leading to slight underestimation in cases involving
 161 blood-filled cavities. In challenging cases with small, entirely blood-filled cavities, segmen-
 162 tation was not possible due to indistinguishable borders. For example, in three exceptional
 163 instances (Case 11 during and after resection, and Case 15 during resection), the cavities
 164 appeared notably small and completely inundated with blood, without any noticeable dark
 165 signals.

166 It is worth noting that, due to the inherent variability in surgical procedures, determin-
 167 ing the precise timing of image capture was challenging since it could occur at different stages
 168 of the resection process. The crucial factor was ensuring that US images were taken before
 169 the surgeon completed the resection entirely, even if residual tumors remained. The segmen-
 170 tation of resection cavities was conducted using ITK-SNAP²⁸. Initially, regularly spaced
 171 slices, approximately one in every five slices, were manually delineated. Subsequently, ITK's
 172 morphological interpolation, facilitated by ITK-SNAP's Convert3D command-line tool, was
 173 utilized to fill in the remaining slices. Convert3D is one of the companion tools of ITK-SNAP
 174 that provides additional features. It is a command-line tool that enables the combination
 175 of multiple image processing tasks into efficient mini-programs, making it an integral tool
 176 in studies involving hundreds of 3D images. In cases where necessary, additional slices were
 177 manually segmented to optimize the interpolation outcome. The segmentation process for
 178 most RESECT cases was originally carried out by two raters as part of a previous study¹⁴.
 179 Following an assessment of intra- and inter-rater variability, these segmentations were re-
 180 viewed by a neurosurgeon and were then modified accordingly. Subsequently, for this study,
 181 the remaining RESECT cases were segmented, and all cases underwent refinement during
 182 the validation protocol detailed in section II.G..

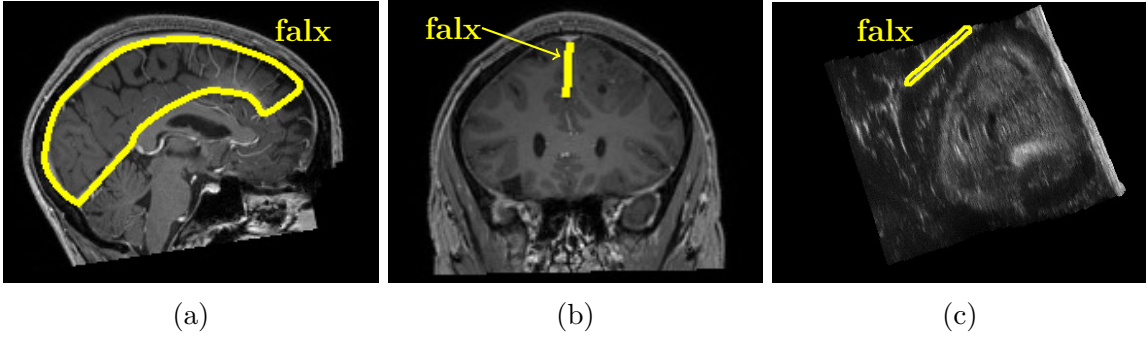


Figure 2: T1 MR (a), (b), and US (c) images of the falx cerebri.

183 II.D. iUS *Falx Cerebri* Segmentation Protocol

184 The *falx cerebri* is the membrane that separates the left and right hemispheres of the brain.
 185 This cerebral falx has a hyperechoic signal in iUS images. It presents a characteristic quasi-
 186 planar shape that appears as a straight line in coronal and axial slices. The falx is also visible
 187 in the MR images, especially T1-weighted (Fig. 2). This structure is thus a convenient
 188 landmark that can be particularly useful to anchor registration. The falx is not always
 189 within the iUS volume due to the limited field of view but can be visible depending on the
 190 tumor location. The falx segmentation is, therefore, present for some volumes only. Since
 191 the falx' bright signal is similar to *sulci* it is difficult to localize the inferior border of the
 192 membrane. We, therefore, used the registered T1-weighted MR images to adjust the falx
 193 segmentation in height. Regularly spaced slices were manually delineated using ITK-SNAP
 194 and then interpolated with Convert3D.

195 II.E. iUS *Sulci* Segmentation Protocol

196 For segmentation purposes, *sulci* were defined as folds filled with cerebrospinal fluid (CSF)
 197 between brain tissue sections. CSF surrounding the brain, such as between the tissue and the
 198 *dura mater* or *tentorium*, was not labeled, although it had a similar iUS signal. *Sulci* were
 199 initially segmented with manual delineation every five slices and morphological interpolation
 200 using Convert3D when moving through the volume in a single direction (e.g., axial slices).
 201 Unlike volumetric structures, *sulci* are thin, complex, folded surfaces. To capture their
 202 irregular shapes, each volume was annotated in three viewing directions (axial, sagittal, and
 203 coronal), and these segmentations were first interpolated separately and later combined into
 204 a union. While this process resulted in slight over-segmentation, it significantly improved
 205 *sulci* delineation, according to annotators and neurosurgeons. In each case, the volume
 206 preceding resection underwent segmentation aided by registered MR images to accurately
 207 delineate *sulci* structures. This initial segmentation served as a reference for segmenting
 208 the volume during and after resection. The manual segmentation process was facilitated by
 209 ITK-SNAP, employing a Wacom One pen tablet, which demonstrated superior speed and
 210 precision compared to a conventional computer mouse.

211 II.F. Pre-operative MR Tumor Segmentation

212 For completeness, we provide segmentations of the tumors in the pre-operative T2 FLAIR
213 images. As the cases in the database are lower-grade gliomas, there is no contrast uptake in
214 the T1 weighted images and the T2 FLAIR images are used to define the tumor boundaries.
215 The tumors were semi-automatically segmented in 3DSlicer using the *GrowCut* algorithm³¹.
216 The resulting segmentations were manually corrected when needed and smoothed with a
217 2×2 mm median filter.

218 II.G. Data Validation

219 All segmentations presented in this work were validated by two experienced neurosurgeons
220 (S.D.R., O.S.). The segmentations were presented to the specialists through a case-by-
221 case 3D Slicer scene, including the original iUS image, segmentation masks, and MR images.
222 Figure 3 represents an example of such a scene. We asked specialists to grade all segmentation
223 masks based on five criteria for three types of structures:

- 224 • Quality of tumor: smoothness of the boundaries (SMT), identification of tumoral tis-
225 sues (IdT), exclusion of non-cancerous tissues (ExT)
- 226 • Quality of resection cavity: identification of resection cavity (IdR)
- 227 • Quality of *sulci* and falx: identification of sulci and falx (IdS)

228 The grading scheme for each criterion was on a scale of 1 to 5 defined as major improvement
229 needed, minor improvement needed, acceptable, good quality, and excellent, respectively.
230 For each criterion, a score of 3 from both surgeons was needed to pass the quality control
231 of segmentation masks. Otherwise, the masks were revised according to the surgeons' com-
232 ments. In determining the choice of a passing score of 3, it is important to clarify that this
233 decision was rooted in the specific criteria established for surgeons evaluating the dataset.
234 The selection of 3 as the pass score was deliberate, as it represented the midpoint on the
235 validation scale of 1 to 5. This choice was informed by the summary of evaluation forms,
236 aiming to identify a common rating among inter-rater assessments. Given the intricate and
237 complex nature of brain structures, achieving consensus on a moderate score like 3 ensured
238 a balanced assessment that accounted for the variability inherent in such evaluations. The
239 final grades for each patient are presented in Table 1.

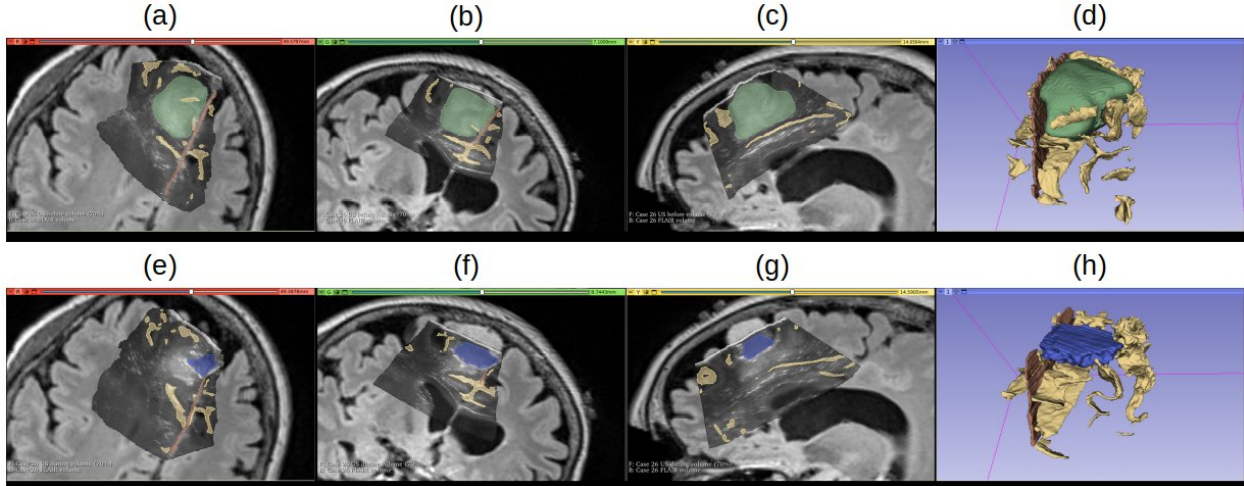


Figure 3: An example of segmentations overlaid with intra-operative ultrasound (iUS) and MR images (green: tumor; yellow: sulci; red: cerebral falx; blue: resection cavity). iUS volume before resection: (a)-(d); iUS volume during resection: (e)-(h).

240 III. Data Format and Usage Notes

241 The proposed RESECT-SEG segmentations are distributed in the NIFTI format. Upon the
 242 acceptance of this paper, they will be available via the OSF open-science [https://osf.io/
 243 jv8bk](https://osf.io/jv8bk) for public viewing and downloading and can be freely used by research laboratories
 244 as well as clinical institutes. However, gaining any financial benefits from the distribution of
 245 the proposed segmentation dataset is prohibited. The database is under the CC BY-NC-SA
 246 4.0 License.

247 IV. Discussion

248 The border and shape of brain tumors have long been established as important diagnostic
 249 markers in resection surgeries. Several image processing techniques have been adopted to
 250 segment tumors which rely on the creation of mathematical descriptions of the tumor border.
 251 Similarly, identifying resection cavity contours has been used to evaluate the completeness
 252 of tumor resection. Finally, segmenting surrounding cerebral structures can greatly bene-
 253 fit image analysis during the surgeries. However, validation of image processing techniques
 254 needs to be investigated in the case of new data. It is important to highlight that there are
 255 few brain datasets accessible to the public, and even those available, such as the BITE²⁴,
 256 RESECT²⁵, and ReMIND²⁶ datasets, do not include iUS segmentation of brain anatomies.
 257 The absence of US segmentation datasets for the brain is largely attributed to the complexity
 258 of the task. To this end, we have provided the manual segmentations of cerebral structures
 259 in iUS images of the 23-patient RESECT dataset, verified by two expert surgeons through
 260 detailed evaluation criteria per brain anatomy. Our proposed expert-annotated RESECT-

261 SEG dataset comprises the segmentation masks of brain tumors, resection cavities, the *falx*
 262 *cerebri*, and *sulci*. Tumor segmentations of the pre-operative MR images are also provided
 263 as a reference. To the best of our knowledge, this is the first study that publicly provides a
 264 comprehensive expert-annotation segmentation of iUS images. The challenging procedure of
 265 delineating brain iUS images has impeded the publications of such segmentations. This vali-
 266 dated dataset serves as a crucial asset for evaluating and benchmarking various segmentation
 267 methods, thereby driving advancements in brain imaging research.

Table 1: Quality control grade chart for segmentation masks before, during, and after resection. Grades of the two neurosurgeons are given side-by-side in each cell. For Case 11 (during and after resection) and Case 15 (during resection), the resection cavity was not labeled (see section II.C).

Validation Scores								
Patient ID	Before Resection				During Resection		After Resection	
	SMT	IdT	ExT	IdS	IdR	IdS	IdR	IdS
1	4 4	4 5	4 3	3 4	3 3	4 4	3 4	4 4
2	4 4	4 3	3 5	4 4	3 4	4 4	3 5	4 5
3	4 4	3 3	4 3	3 3	3 4	3 3	4 4	4 3
4	3 4	3 5	4 5	3 4	3 4	4 4	4 5	3 4
5	3 4	4 4	4 4	3 4	3 5	3 4	4 5	4 3
6	3 4	4 5	3 5	3 4	4 5	4 4	4 5	4 4
7	3 4	3 5	4 4	3 4	3 3	4 4	4 5	4 4
8	4 3	4 4	4 5	3 4	3 5	3 4	3 5	4 4
11	4 4	4 4	3 5	4 4	- -	4 3	- -	4 3
12	3 4	4 3	4 3	4 4	3 4	3 4	4 5	4 5
13	4 4	4 4	3 4	4 3	3 5	4 5	3 5	4 3
14	4 4	3 4	4 4	4 4	4 3	4 4	4 4	3 4
15	3 4	3 3	4 3	4 4	- -	4 4	4 4	4 4
16	4 4	4 4	4 4	4 4	3 4	4 4	3 4	3 4
17	3 4	4 5	4 5	4 4	4 5	4 4	3 4	4 4
18	4 4	3 4	3 4	4 4	3 4	3 4	3 5	3 5
19	3 4	3 5	3 5	4 3	3 5	3 5	3 5	4 4
21	3 4	3 4	4 4	3 4	4 5	4 4	4 5	4 4
23	3 4	3 5	3 5	3 4	3 3	4 4	3 5	4 4
24	4 4	4 4	3 5	3 5	3 4	4 4	3 4	4 4
25	4 4	3 4	3 4	3 4	4 3	3 4	3 4	3 3
26	4 5	4 5	3 5	3 5	3 5	3 5	3 5	3 3
27	4 5	3 3	3 5	4 4	3 3	3 4	3 5	3 4

SMT: smoothness of the boundaries, IdT: identification of tumoral tissues, ExT: exclusion of non-cancerous tissues, IdS: identification of sulci and falx. IdR: identification of resection cavity

268 The proposed RESECT-SEG dataset offers substantial utility, focusing primarily on
 269 two pivotal applications that have the potential to revolutionize brain tumor diagnosis and

270 treatment. As the first application, it accelerates the development of advanced image analy-
271 sis algorithms for brain tumor detection and segmentation, whether based on deep learning
272 or energy minimization. With the growing number of segmentation algorithms, there is
273 a need for comprehensive evaluation, and this dataset provides a standardized metric for
274 rigorous testing, propelling advancements in brain cancer treatment. Therefore, the pro-
275 posed dataset offers an opportunity for both technical and clinical communities to rigor-
276 ously test their algorithms. Additionally, it offers a unique opportunity for algorithms to
277 excel in multi-instance detection and segmentation, enhancing performance beyond binary
278 segmentation tasks. Multiple methodologies are available for binary segmentation problems;
279 however, recent studies suggest that integrating instances into deep learning algorithms not
280 only enhances performance through parallel multi-instance segmentation but also achieves
281 a comprehensive improvement overall³². Consequently, this dataset acts as a catalyst in
282 refining computer-aided diagnosis (CAD) systems, enabling multi-instance and multi-organ
283 analyses, thereby revolutionizing brain tumor diagnosis and treatment.

284 The second application is transformative, focusing on developing and validating
285 segmentation-based registration algorithms to address brain shift challenges during surgery.
286 Brain shift, involving tissue deformation and displacement, poses precision hurdles in surgery.
287 Integrating this dataset into registration algorithms provides them with expert-annotated
288 tumor segmentations as a foundation. These resources empower algorithms to dynamically
289 recalibrate pre-operative images in real-time, aligning them with evolving intraoperative con-
290 ditions. The result is an advanced neuronavigation system, offering surgeons accurate, real-
291 time patient anatomical visualization. This leads to enhanced resection control, minimizing
292 structural damage risk and optimizing tumor removal. The synergy between segmentation
293 and registration algorithms has the potential to redefine neurosurgery, equipping surgeons
294 with a powerful tool to navigate brain shift complexities, ultimately ensuring safer surgeries,
295 better patient outcomes, and improved resection control. This advancement holds promise
296 for revolutionizing the field of neurosurgery.

297 The proposed RESECT-SEG dataset stands as a pivotal resource for advancing image
298 processing techniques in neurosurgery. While it offers valuable segmentations of cerebral
299 structures, it's essential to acknowledge its limitations. One such concern is the potential
300 lack of representation of diverse clinical scenarios. Ensuring the dataset encapsulates a broad
301 spectrum of anatomical variations, tumor types, and imaging modalities is crucial for its
302 relevance and applicability in broader contexts. Evaluating the generalizability of proposed
303 techniques beyond the confines of the RESECT-SEG dataset is imperative. Nevertheless,
304 by adhering to rigorous evaluation protocols, conducting thorough validation processes, and
305 maintaining transparent reporting standards, the RESECT-SEG dataset can significantly
306 improve its credibility and impact in advancing neurosurgical image processing techniques.

307 V. Conclusion

308 In this study, the most comprehensive and validated expert delineations of cerebral structures
309 within iUS images from the RESECT database were proposed. The primary focus lay in

310 outlining tumor boundaries within pre-resection iUS 3D volumes and tracking the resection
311 cavity both during and post-surgery. Additionally, delineated *sulci* and the *falx cerebri* were
312 further provided to enhance surgical precision. This dataset presents an invaluable resource
313 for both the training and evaluation of DL-based segmentation algorithms and registration
314 methodologies, thereby presenting a rigorous challenge to their capabilities. This collective
315 effort is poised to catalyze advancements in brain tumor treatment and surgical interventions,
316 ultimately benefiting patients and furthering the realm of medical science.

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