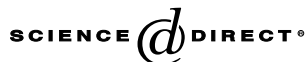




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2 A brain tumor segmentation framework based on outlier detection ☆

3 Marcel Prastawa ^{a,*}, Elizabeth Bullitt ^c, Sean Ho ^a, Guido Gerig ^{a,b}

4 ^a Department of Computer Science, University of North Carolina, CB #3175, Sitterson Hall, Chapel Hill, NC 27599, USA

5 ^b Department of Psychiatry, University of North Carolina, Chapel Hill, NC 27599, USA

6 ^c Department of Surgery, University of North Carolina, Chapel Hill, NC 27599, USA

Abstract

9 This paper describes a framework for automatic brain tumor segmentation from MR images. The detection of edema is done
10 simultaneously with tumor segmentation, as the knowledge of the extent of edema is important for diagnosis, planning, and
11 treatment. Whereas many other tumor segmentation methods rely on the intensity enhancement produced by the gadolinium
12 contrast agent in the T1-weighted image, the method proposed here does not require contrast enhanced image channels. The only
13 required input for the segmentation procedure is the T2 MR image channel, but it can make use of any additional non-enhanced
14 image channels for improved tissue segmentation. The segmentation framework is composed of three stages. First, we detect ab-
15 normal regions using a registered brain atlas as a model for healthy brains. We then make use of the robust estimates of the location
16 and dispersion of the normal brain tissue intensity clusters to determine the intensity properties of the different tissue types. In the
17 second stage, we determine from the T2 image intensities whether edema appears together with tumor in the abnormal regions.
18 Finally, we apply geometric and spatial constraints to the detected tumor and edema regions. The segmentation procedure has been
19 applied to three real datasets, representing different tumor shapes, locations, sizes, image intensities, and enhancement.
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21 *Keywords:* Automatic brain segmentation; Brain tumor segmentation; Level-set evolution; Outlier detection; Robust estimation

22 1. Introduction

23 Automatic brain tumor segmentation from MR im-
24 ages is a difficult task that involves various disciplines
25 covering pathology, MRI physics, radiologist's percep-
26 tion, and image analysis based on intensity and shape.
27 There are many issues and challenges associated with
28 brain tumor segmentation. Brain tumors may be of any
29 size, may have a variety of shapes, may appear at any
30 location, and may appear in different image intensities.
31 Some tumors also deform other structures and appear
32 together with edema that changes intensity properties of
33 the nearby region. For many human experts, manual
34 segmentation is a difficult and time consuming task,
35 which makes an automated brain tumor segmentation
36 method desirable. There are many possible applications
37 of an automated method, it can be used for surgical

planning, treatment planning, and vascular analysis. It 38
has been shown that blood vessels in the brain exhibit 39
certain characteristics within pathological regions (Bul- 40
litt et al., 2003). An objective and reproducible seg- 41
mentation procedure coupled with vascular analysis 42
would allow us to study the relation between patholo- 43
gies and blood vessels and may function as a new di- 44
agnostic measure. 45

The challenges associated with automatic brain tu- 46
mor segmentation have given rise to many different 47
approaches. Automated segmentation methods based 48
on artificial intelligence techniques were proposed in 49
(Clark et al., 1998; Fletcher-Heath et al., 2001). The two 50
methods do not rely on intensity enhancements provided 51
by the use of contrast agents. A particular limitation of 52
the two methods is that the input images are restricted to 53
the T1, T2, and PD MR image channels. Additionally, 54
the methods require a training phase prior to segment- 55
ing a set of images. Other methods are based on statisti- 56
cal pattern recognition techniques, for example the 57
method proposed by Kaus et al. (1999). This method 58
combines the information from a registered atlas tem- 59

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* Corresponding author. Tel.: +919-962-1836.

E-mail address: prastawa@cs.unc.edu (M. Prastawa).

60 plate and user input to supervise training of a the clas-
61 sifier, demonstrating the strength of combining voxel-
62 intensity with geometric brain atlas information. This
63 method was validated against meningiomas and low-
64 grade gliomas. Gering et al. (2002) proposed a method
65 that detects deviations from normal brains using a
66 multi-layer Markov random field framework. The in-
67 formation layers include voxel intensities, structural
68 coherence, spatial locations, and user input. Cuadra
69 et al. (2002) presented high-dimensional warping to
70 study deformation of brain tissue due to tumor growth.
71 This technique relies on a prior definition of the tumor
72 boundary whereas the method we propose in this paper
73 focuses on automatically finding tumor regions.

74 Previous work on automatic brain tumor segmenta-
75 tion generally uses the enhancement provided by the
76 gadolinium contrast agent in the T1 channel or con-
77 strained to blobby shaped tumors with uniform inten-
78 sity. Even though the intensity enhancement can aid the
79 segmentation process, it is not always necessary to ob-
80 tain good results. In fact, the use of a contrast agent can
81 be problematic. Typically, tumors are only partially
82 enhanced and some tumors are not enhanced at all.
83 Blood vessels also generally appear enhanced by the
84 contrast agent. These inconsistencies create an ambigu-
85 ity in the image interpretation, which makes the T1-
86 enhanced image channel a less than ideal feature for
87 tumor segmentation.

88 Edema surrounding tumors and infiltrating mostly
89 white matter was most often not considered as impor-
90 tant for tumor segmentation. We showed previously
91 (Moon et al., 2002; Prastawa et al., 2003) that edema
92 can be segmented using a prior for edema intensity and
93 restriction to the white matter region. The extraction of
94 the edema region is essential for diagnosis, therapy
95 planning, and surgery. It is also essential for attempts
96 that model brain deformation due to tumor growth. The
97 swelling produced by infiltrating edema usually has
98 distinctly different tissue property characteristics than
99 tumor. Our new scheme presented here is based on the
100 detection of “changes from normal” and will thus sys-
101 tematically include segmentation of edema. Differential
102 identification of the two abnormal regions tumor and
103 edema is clinically highly relevant. Even though the
104 primary therapeutic focus will be on the tumor region,
105 the edema region may require secondary analysis and
106 treatment.

107 Our method combines the model of the normal tis-
108 sues and the geometric and spatial model of tumor and
109 edema. It relies on the information provided in the T2
110 image channel for identifying edema, and it can make
111 use of additional image channels to aid the segmenta-
112 tion. For our datasets, we use only the T1 and T2
113 channels. Tumor and edema are treated as intensity
114 abnormalities or outliers. After identifying the abnor-
115 malities, an unsupervised clustering technique is applied

116 to the intensity features before utilizing geometric and
117 spatial constraints. We will demonstrate that this
118 method can segment tumors with or without intensity
119 enhancements and automatically detects the presence of
120 edema, thus overcoming limitations of our previous
121 method (Moon et al., 2002; Prastawa et al., 2003). Our
122 approach offers a means of approaching lesions of
123 multiple types and image intensities, and, with a single
124 method, lesions that enhance and do not, and that may
125 or may not be surrounded by edema.

2. Method 126

127 The automated segmentation method that we have
128 developed is composed of three major stages, as shown
129 in Fig. 1. First, it detects abnormal regions, where the
130 intensity characteristics deviate from the expectation. In
131 the second stage, it determines whether these regions are
132 composed of both tumor and edema. Finally, once the
133 estimates for tumor and edema intensity parameters are
134 obtained, the spatial and geometric properties are used
135 for determining proper sample locations. The details of
136 each stage are discussed in the following subsections.

2.1. Detection of abnormality 137

138 Before identifying tumor and edema, it is necessary to
139 first detect regions that have properties that deviate
140 from the expected properties of a normal, healthy brain.
141 In our segmentation method, this involves finding the
142 intensity parameters for healthy classes and the abnor-
143 mal class. The initial parameters for the healthy brain
144 classes are obtained by sampling specific regions based
145 on the probabilistic brain atlas shown in Fig. 2 (Evans
146 et al., 1993).

147 The atlas is aligned with the subject image data by
148 registering the atlas template image with the subject
149 image. The registration is performed using affine trans-
150 formation with the mutual information image match

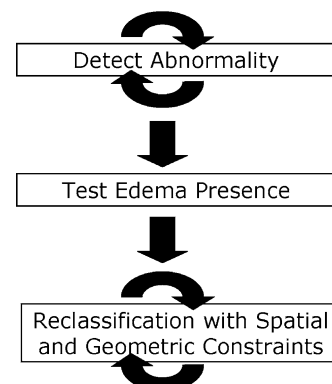


Fig. 1. The three major stages of the segmentation method.

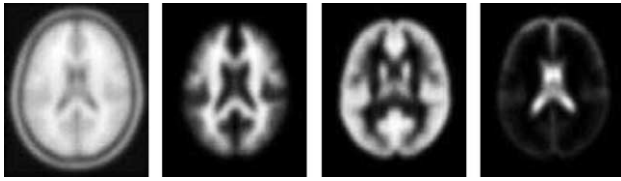


Fig. 2. The digital brain atlas provided by the International Consortium for Brain Mapping (ICBM). From left to right: the T1 template image and probability values of white matter, gray matter, and csf.

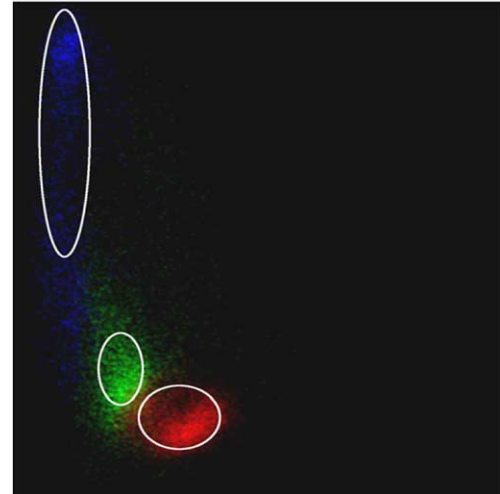
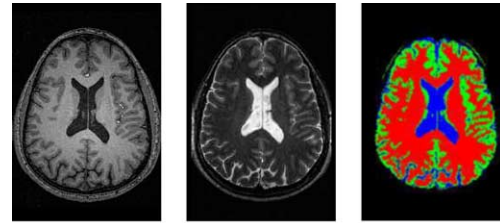


Fig. 3. Example healthy dataset. Top, from left to right: T1 image, T2 image, and segmentation labels (from brightest to darkest: white matter, gray matter, and csf). Bottom: the intensity histogram for the three classes, the horizontal axis represents T1 intensities and the vertical axis represents T2 intensities. The intensity features for each class is tightly clustered and can be approximated with a Gaussian. (This figure is available in color, see the online version.)

151 measure (Maes et al., 1997). After alignment, the sam-
152 ples for each healthy class (white matter, gray matter,
153 and cerebrospinal fluid (csf)) are obtained by randomly
154 selecting the voxels with high atlas probability values.
155 For our data, the set of training samples is constrained
156 to be the voxels with probabilities higher than a
157 threshold $\tau = 0.85$.

158 The training data for the healthy classes generally
159 contain unwanted samples due to contamination with
160 samples from other tissue types, particularly tumor and
161 edema. The pathological regions are not accounted for
162 in the brain atlas and they therefore occupy regions that
163 are marked as healthy. The contaminants are data
164 outliers, and they are removed so that the training
165 samples for the healthy classes are not contaminated.
166 The samples are known to be contaminated if their
167 characteristics differ from prior knowledge. The inten-
168 sities for healthy classes are known to be well clustered
169 and can be approximated using Gaussians (Fig. 3).

170 Handling data outliers is a crucial step for atlas based
171 image segmentation. Cocosco et al. (2003) developed a
172 segmentation method for healthy brains that builds the
173 Minimum Spanning Tree from the training samples and
174 iteratively breaks the edges to remove false positives
175 (pruning). They showed that pruning the training sam-
176 ples results in significant improvement of the segmen-
177 tation quality. We use a robust estimate of the mean and
178 covariance of the training data to determine the outliers
179 to be removed.

180 The robust estimator that we use is the Minimum
181 Covariance Determinant (MCD) estimator. It is defined
182 to be the mean and covariance of an ellipsoid covering
183 at least half of the data with the lowest determinant of
184 covariance. The method is highly robust, with a high
185 breakdown point. The breakdown point is the fraction
186 of the data that must be moved to infinity so that the
187 estimate also moves to infinity. The MCD estimate has a
188 breakdown point of 0.5, more than half of the data
189 needs to be contaminated to make the estimate be un-
190 reasonable.

191 A fast algorithm for computing the MCD estimate is
192 described in (Rousseeuw and Van Driessen, 1999). The
193 algorithm first creates several initial subsets, where the
194 elements are chosen randomly. From each subset,
195 the algorithm determines different initial estimates of the

robust mean and covariance. The estimates are then 196
refined by performing a number of C-step operations on 197
each initial selections. A single C-step operation consists 198
of the following steps: 199

- 200 (1) Given a subset of the data, compute the mean and 201
covariance of the elements in the subset. 202
- 203 (2) Compute Mahalanobis distances of the data ele- 204
ments in the whole set. 205
- 206 (3) Sort points based on distances, smallest to largest. 207
- 208 (4) Select a new subset where the distances are mini- 209
mized (e.g., first half of the sorted data points). 210

211 An illustration of a single C-step iteration is shown in 212
Fig. 4. A C-step operation will result in a subset selection 213
that yields a determinant of covariance less or equal 214
to the one obtained from the previous subset. The iterative 215
applications of C-steps yield final estimates with 216
the smallest determinant of covariance. From all the 217
final estimates computed with different initial selections, 218
the mean and covariance estimate with the smallest de- 219
terminant of covariance is chosen as the robust estimate. 220
Given the robust mean and covariance, samples that are
further than three standard deviations are considered as
outliers (Fig. 5). The inliers of the healthy brain tissue
class samples are used as training samples for estimating
the corresponding density functions.

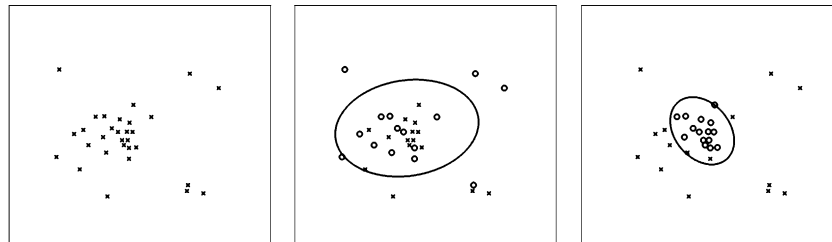


Fig. 4. An illustration of a single C-step iteration, a key component of the MCD robust estimation algorithm. Left: original 2-D data. Center: random selection of a subset of the data (marked with circles). Right: the selection after a C-step iteration, where the closest points to the previous mean and covariance estimate is selected. The ellipsoidal curves in the center and right plots show the locations one standard deviation away from the mean and covariance estimate, which are computed from the selected points.

221 The specific aim at this stage is to compute the density
 222 estimates and posterior probabilities for the class labels
 223 $\Gamma = \{\text{white matter, gray matter, csf, abnormal, non-}$
 224 $\text{brain}\}$. A parametric density function is not ideal for the
 225 case of tumor segmentation. Tumors do not always
 226 appear with uniform intensities, particularly in the case
 227 where some tissues inside the tumor are necrotic tissues.
 228 We therefore make no assumption regarding the inten-
 229 sity distributions and use a non-parametric model for
 230 the probability density functions. The density functions
 231 are approximated using kernel expansion or Parzen
 232 windowing (Duda et al., 2001). Given the vector of inten-
 233 sities $\vec{I}(x)$ at location x , the probability density
 234 function on intensity for the class label Γ_j is

$$p(\vec{I}(x)|\Gamma_j) = \frac{1}{N} \sum_{i=1}^N K_\lambda(\vec{I}(x) - \vec{T}_i),$$

236 where K_λ is the multivariate Gaussian kernel with
 237 standard deviation λ and \vec{T}_i is a class training sample.
 238 The kernel bandwidth λ chosen for our dataset is 4% of
 239 the intensity range for each channel.

240 The posterior probability is computed using the class
 241 prior probability from the atlas $Pr(\Gamma_j, x)$ at location x

$$P(\Gamma_j|\vec{I}(x)) = \frac{p(\vec{I}(x)|\Gamma_j)Pr(\Gamma_j, x)}{p(\vec{I}(x))}.$$

243 The spatial priors for white matter, gray matter, csf,
 244 and non-brain classes are the corresponding atlas

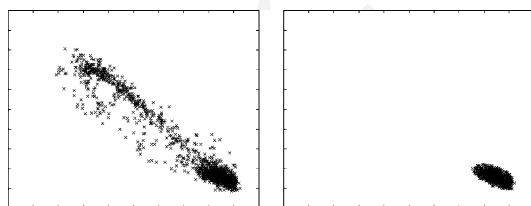


Fig. 5. The white matter training data for a subject with tumor and edema, the horizontal axis represents the T1 intensities and the vertical axis represents the T2 intensities. Left: original samples obtained by atlas-guided sampling which is contaminated with samples from other distributions. Right: remaining samples after trimming using the robust MCD estimate.

245 probabilities. For the abnormal class, we use a fraction
 246 of the sum of white matter and gray matter atlas
 247 probabilities since tumor and edema usually appear in
 248 these regions and not in the csf regions.

249 An issue with MR images is the presence of the image
 250 inhomogeneity or the bias field. We deal with this by
 251 interleaving the segmentation process with bias correc-
 252 tion, following the spirit of (Wells et al., 1996). The
 253 entire process of detecting the abnormal regions is
 254 shown in Fig. 6, a loop that is composed of the following
 255 five stages:

- 256 (1) Threshold the posterior probabilities and sample the
 257 high confidence regions. At the first pass, the atlas
 258 probabilities are used in place of the posterior prob-
 259 abilities.
- 260 (2) Remove the samples for normal tissues that exceed a
 261 distance threshold based on the MCD estimate.
- 262 (3) Estimate the non-parametric density for each class
 263 labels using kernel expansions. The initial density
 264 for the abnormal class is set to be uniform, which
 265 makes this class act as a rejection class. The brain
 266 voxels with intensity features that are different from
 267 those of healthy classes or not located in the ex-
 268 pected spatial coordinates will be assigned to this
 269 class.
- 270 (4) Compute the posterior probabilities.

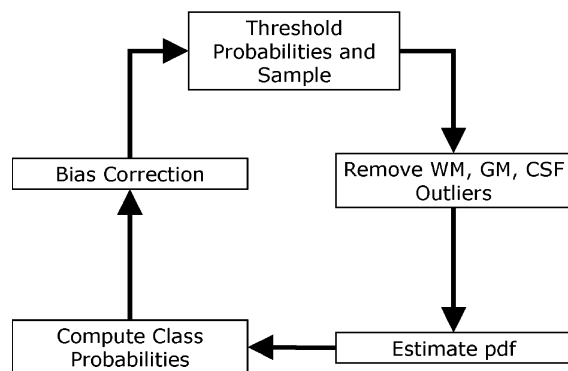


Fig. 6. The process of detecting abnormal regions, the first stage of the method.

271 (5) Estimate bias field from white matter and gray mat-
272 ter probabilities. Apply correction using the esti-
273 mated bias field.

274 The first major segmentation stage detects the ab-
275 normal regions by executing the loop for several itera-
276 tions, obtaining the intensity descriptions for each class.
277 The abnormal class density at different iterations for the
278 Tumor020 data is shown in Fig. 7.

279 The bias correction method is based on the one de-
280 veloped by Van Leemput et al. (1999). The method uses
281 the posterior probabilities to estimate the homogeneous
282 image. It then computes the bias field estimate, as the
283 log-difference between the homogeneous images and the
284 real subject images. The bias field is modeled as a
285 polynomial, and the coefficients of the polynomial is
286 determined through least squares fitting. The method
287 assumes that the class intensity distributions are ap-
288 proximately Gaussians. We therefore use only the white
289 matter and gray matter probabilities for bias correction,
290 as they generally can be approximated by Gaussians
291 without significant errors.

292 2.2. Detection of edema

293 The densities and posterior probabilities computed
294 for the abnormal class in the previous stage give us a
295 rough estimate of how likely it is that some voxels are
296 part of tumor or edema. We assume that the detected
297 abnormal voxels are composed mostly of tumor and
298 possibly edema. Edema is not always present when tu-
299 mor is present, therefore it is necessary to specifically
300 test the presence of edema. This is done by first ob-
301 taining the intensity samples for the abnormal region,
302 the posterior probabilities are thresholded and a subset
303 of the region is selected. The samples are clustered and
304 then we determine whether there exist separate clusters
305 for tumor and edema. The density estimate for tumor
306 (and edema, if present) is obtained by performing kernel
307 expansion on the samples.

308 Tumor and edema are generally separable given the
309 information in the T2 weighted image (Fig. 8). Edema

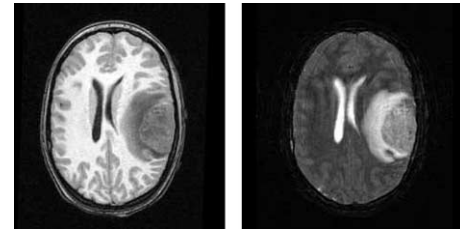


Fig. 8. The T1 image (left) and the T2 image (right) from the Tumor020 data. The tumor and edema on the right part of the brain can be clearly differentiated based on the T2 intensities. As observed in the T2 image, the tumor region (rightmost) is darker than the surrounding edema region, as edema is composed mostly of fluid.

has high fluid content and therefore appears brighter than tumor in this image channel. To separate the densities, we apply unsupervised clustering to the samples obtained by thresholding. The method we have chosen is k -means clustering with $k = 2$ (Duda et al., 2001). Once we obtain the clusters, we can identify the tumor cluster as the cluster with the T2 mean that has the lower value.

To determine the validity of the clustering, we use the overlap measure called the Davies–Bouldin index (Davies and Bouldin, 1979). This measure is the ratio of the average within cluster distances and the between cluster distance. Given m candidate tumor samples τ_i with the mean value μ_{tumor} , and n candidate edema samples ϵ_i with the mean value μ_{edema} , the overlap measure is

$$\frac{1}{2} \left(\frac{\frac{1}{m} \sum_{i=1}^m \|\tau_i - \mu_{\text{tumor}}\| + \frac{1}{n} \sum_{i=1}^n \|\epsilon_i - \mu_{\text{edema}}\|}{\|\mu_{\text{tumor}} - \mu_{\text{edema}}\|} \right).$$

The T2 channel contains most of the information needed for differentiating tumor and edema. Therefore, we have chosen to measure the overlap for only the T2 data of each cluster. If the amount of overlap is larger than a specified threshold, then the tumor density is set to be the density for the abnormal class and the edema density is set to zero.

2.3. Reclassification with spatial and geometric constraints

Once this stage is reached, tumor and edema are already segmented based on atlas priors and intensity characteristics. However, the geometric and spatial properties were not considered and this generally leads to having at least a few false positives. Since there is no model for the intensity distributions of tumor and edema, it is necessary to use geometric and spatial heuristics to prune the samples that are used for estimating the densities. Here, we make use of the prior knowledge that tumor is mostly blobby. For edema, we use the constraint that each edema region is connected to a nearby tumor region. Some edema voxels can be located far

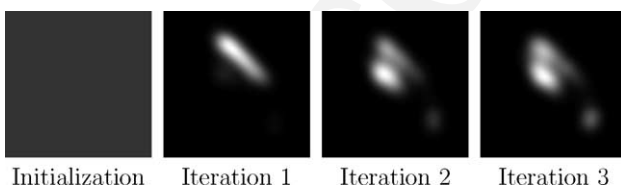


Fig. 7. Snapshots of the estimated probability density function of the abnormal class for the Tumor020 data. Each image shows the result of different iterations of the loop shown in the previous figure. The density is initialized so that all intensities are equally likely. The horizontal axis represents the T1 intensities and the vertical axis represents the T2 intensities. The two high density regions visible at the final iteration are the tumor and edema densities, which have a significant separation along the dimension of the T2 intensities.

away from tumor regions, but they must be connected to a tumor region spatially.

Tumor structures generally appear as blobby lumps, this shape constraint is enforced through region competition snakes (Sebastian et al., 2003; Tek and Kimia, 1995; Tek and Kimia, 1997; Zhu et al., 1995). The tumor posterior probabilities is used as the input for the snake, which is represented as the zero level set of the implicit function ϕ . The level set evolution is governed by the following equation (Ho et al., 2002):

$$\frac{\partial \phi}{\partial t} = \alpha(P(\text{tumor}|\vec{I}(x)) - P(\overline{\text{tumor}}|\vec{I}(x)))|\nabla \phi| + \beta \nabla \cdot \left(\frac{\nabla \phi}{|\nabla \phi|} \right) |\nabla \phi|.$$

The propagation term is represented by α . It is modulated by the difference of the posterior probabilities for the tumor class and the non-tumor class ($P(\text{tumor}|\vec{I}(x))$ and $P(\overline{\text{tumor}}|\vec{I}(x))$), so that the direction of the propagation is determined by the sign of the difference. The probability that a voxel is part of brain and not part of tumor is represented by $P(\overline{\text{tumor}}|\vec{I}(x))$, more explicitly

$$P(\overline{\text{tumor}}|\vec{I}(x)) = P(\text{wm}|\vec{I}(x)) + P(\text{gm}|\vec{I}(x)) + P(\text{csf}|\vec{I}(x)) + P(\text{edema}|\vec{I}(x))$$

The snake shrinks when the boundary encloses part of the regions not part of tumor and expands when the boundary is inside the tumor region. We apply a smoothing on the snake contour using mean curvature flow, and the strength of this smoothing is controlled by the β term. The initial level set function is obtained by performing a distance transform on the segmented tumor objects.

Edema, if present, is always contiguous with the tumor. With this prior knowledge, we therefore assume that edema is located near tumor structures. Each segmented edema object must have a voxel that is no further than some small distance from tumor regions. This test can be done efficiently by using the connected component algorithm and mathematical morphology. We first generate a binary image representing the segmented edema region. Then, we use this image as an input for the connected component algorithm to determine the individual edema objects. Each object is then dilated with a small structuring element, and then compared against the segmented tumor regions. The objects that share at least a voxel with a tumor region is considered valid. Edema samples from these regions are kept, while other edema samples are discarded.

The final segmentation is obtained by reclassifying the image using the iterative steps similar to the one described in Section 2.1, with some modifications (Fig. 9). The outlier removal stage is removed and there are additional steps where these geometric and spatial

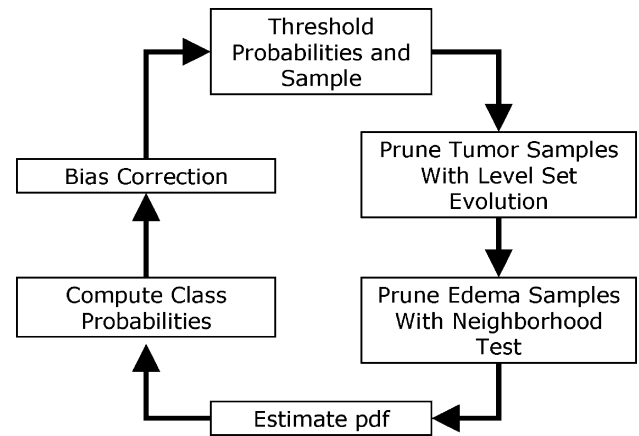


Fig. 9. The third stage of the method where the image is reclassified using tumor geometric properties and edema spatial relation.

constraints are enforced. The entire loop is performed several times, after going through one loop the tumor and edema probabilities at the voxel locations that do not pass the tests to zero. This way, the segmentation for these locations are determined based on the next best candidate class. The tumor shape constraint is disabled at the last fitting stage. This is done to obtain the proper boundary for the tumor structures, which may not be entirely smooth. For instance, gliomas typically have a general blobby shape and ragged boundaries.

3. Results

We have applied the method to three real datasets, representing different tumor shapes, locations, sizes, image intensity, and enhancement, as shown in Fig. 10. Tumor020 has a partially enhancing tumor that causes a large deformation of the normal structures. Tumor025 contains a large, partially enhancing tumor inside the brain stem. Tumor033 contains a low grade tumor which is not highlighted in the T1-enhanced channel.

Two sets of segmentations are done manually by one human rater at different times. The volumes of the manually segmented structures are shown in Table 1. The first set of manual segmentations is considered to be the gold standard for validating the automatic segmentation method. We used the VALMET segmentation validation tool (Gerig et al., 2001) to generate five validation metrics. The volume overlap metric is the normalized voxel intersection count for the pair of segmentations A and B : $(A \cap B)/(A \cup B)$, otherwise known as Jaccard's similarity coefficient (Jaccard, 1912). The other metrics are the maximum Hausdorff surface distance and the average surface distances (inside/negative, outside/positive, and absolute).

The intra-rater variability is shown in Table 2. The surface distance metrics indicate that the manual seg-

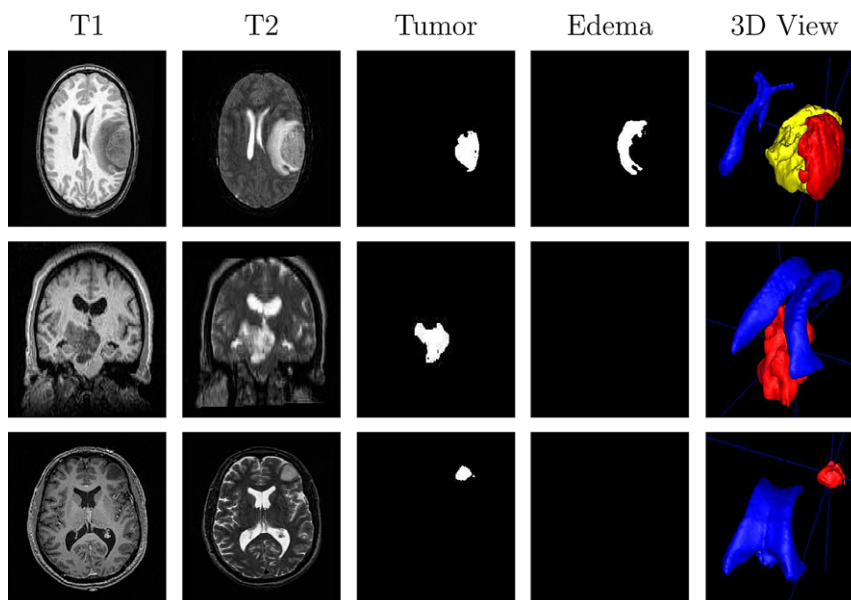


Fig. 10. The datasets and the generated segmentation results. The last column shows the 3D views of the segmented structures: medium gray represents tumor, bright gray represents edema, and dark gray represents ventricles. From top to bottom: Tumor020, Tumor025, Tumor033. These results illustrate that our method does differential segmentation for tumor and edema, which works also in cases where no edema is present. (This figure is available in color, see the online version.)

Table 1
Volumes of the segmented structures, from the first set of manual segmentation results

Dataset	Tissue type	Volume (mm ³)
Tumor020	Tumor	35578.6
Tumor020	Edema	64860.6
Tumor025	Tumor	24742.4
Tumor033	Tumor	3661.5

431 mentations are reliable. The overlap metrics are also
 432 high, with the exception of the Tumor033 segmentation.
 433 This is likely due to the small size of the tumor. The
 434 quantitative validation of the automatic segmentation
 435 method is shown in Table 3. The level of agreement
 436 based on surface distances is similar for all tumors.
 437 However, the varying overlap values demonstrate that
 438 the overlap metric is sensitive to the size and complexity
 439 of the segmented objects (Fig. 10). The level of agree-
 440 ment with the manual result for edema is lower than
 441 tumor. This is mainly due to the ambiguity in deter-
 442 mining the edema boundary, especially the tumor–ede-

ma boundary. For each case, the time required for the 443
 automatic segmentation method is about 1 h 30 min on 444
 a 2 GHZ Intel Xeon machine. The automatic segmen- 445
 tation process is done with little user intervention. The 446
 user only needs to specify several parameters before the 447
 segmentation begins. These parameters include the atlas 448
 probability threshold, the level set evolution settings, 449
 kernel width for Parzen windowing, and the distance 450
 threshold for outlier detection. 451

4. Discussion 452

4.1. Application areas 453

The automatic segmentation method proposed in this 454
 paper can process a wide variety of tumors since it does 455
 not rely on contrast enhancement. It segments the whole 456
 brain, including healthy tissue types, and automatically 457
 identifies edema. Defining the edema region can be 458
 useful for surgical planning, definition of radiation 459
 therapy fields, and, since the edema region indicates the 460
 volume over which the tumor exerts obvious chemical 461

Table 2
Validation metrics comparing the two sets of manual segmentation results done by the same human rater, demonstrating the intra-rater variability of the manual segmentations

Dataset	Tissue type	Overlap (%)	Hausdorff (mm)	Inside (mm)	Outside (mm)	Absolute (mm)
Tumor020	Tumor	89.0	3.98	0.32	1.17	0.54
Tumor020	Edema	75.5	13.1	0.48	1.4	0.75
Tumor025	Tumor	81.2	4.1	0.21	1.31	0.73
Tumor033	Tumor	59.4	5.22	0.42	2.06	1.51

Table 3

Validation metrics of the automatic tumor segmentation results against the first set of manual segmentation results

Dataset	Tissue type	Overlap (%)	Hausdorff (mm)	Inside (mm)	Outside (mm)	Absolute (mm)
Tumor020	Tumor	80.0	16.79	1.28	2.16	1.64
Tumor020	Edema	68.2	12.80	0.63	2.43	1.75
Tumor025	Tumor	79.2	17.85	1.01	3.70	1.44
Tumor033	Tumor	70.6	8.60	0.25	2.47	1.85

462 effects, identification of areas of interest to multiple in-
463 vestigators interested in tumor growth and treatment.
464 Knowing the edema region can also be useful for sur-
465 gical planning and radiation therapy. Often, edema re-
466 gions need to be treated to reduce the risk of recurrence.

467 4.2. Future work

468 The segmentation method presented in this paper
469 detects abnormal regions in the brain based on the atlas
470 and image intensities. Other properties can also be used
471 for this process. This can include geometric properties
472 such as curvature or brain asymmetry (Joshi et al.,
473 2003). Although the contrast enhanced image channel
474 leads to ambiguous information, there are cases where it
475 leads to more straightforward identification of brain
476 tumors, assuming that enhanced blood vessels and noise
477 can be properly identified. Robust estimation schemes
478 other than the MCD may be necessary for these exten-
479 sions.

480 A potential issue that is not handled by the proposed
481 method is large deformation of brain structures. When
482 there is large deformation, the brain atlas used may lead
483 to incorrect sampling. In this case, the atlas based
484 samples would be severely contaminated and the MCD
485 algorithm may not yield correct results. The spatial
486 priors here would also limit the segmentation quality, as
487 the segmentation output cannot differ greatly from the
488 atlas. The current method can still handle some level of
489 deformation due to the use of outlier detection, but it
490 would be helpful to explicitly account for these defor-
491 mations using deformable registration.

492 An issue that goes together with the issue of knowing
493 the deformation induced by tumor is the problem of de-
494 termining the possible shapes of brain tumors. The shape
495 model for tumor enforced using region competition snake
496 constrains the segmented tumor to have rather smooth
497 shapes. The notion of spatial coherence for brain tumors
498 need to be properly enforced in order to segment wider
499 varieties of brain tumors. This is a difficult issue because
500 tumors can appear in many different sizes and shapes.

501 5. Conclusion

502 This paper presents a new approach for automatic
503 segmentation of tumors and adjoining edema from non-

enhancing multichannel MRI (T2 weighted channel ex- 504
plicitly required). Most methods so far have been ap- 505
plicable only to enhancing, homogeneous tumors. 506
Furthermore, they require user-guidance in training a 507
supervised classifier or to obtain a rough outline of the 508
region of interest. Here, we show that robust estimation 509
and outlier detection can be a promising new concept 510
for detecting abnormalities in the brain. 511

The presented technique automatically identifies the 512
presence of edema. Our collaborating clinicians confirm 513
that this is a highly relevant feature, as the edema region 514
often may require secondary analysis and treatment af- 515
ter the primary focus to the tumor region. The technique 516
uses a concept that detects *difference from normal* and 517
uses non-parametric estimates for distributions rather 518
than traditional mixture Gaussian models. The techni- 519
que also makes use of other features besides intensity: 520
the shape of brain tumor and location of edema. In the 521
future, we will improve this framework so that it 522
can segment wider varieties of brain tumors with and 523
without edema. 524

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