RESEARCH ARTICLE

OPEN ACCESS

A Survey of Brain Tumor Segmentation Methods with Different Image Modalitites

M. Sumithra^[1], S. Malathi^[2] Ph.D Scholar^[1] Sathyabama University Dean of M.E, Professor^[2] Panimalar Engineering Collage Chennai – India

ABSTRACT

Brain tumor segmentation is a critical strategy for early tumor determination and radiotherapy arranging. Upgrading tumor segmentation strategies is as yet difficult in light of the fact that brain tumor images show complex qualities, for example, high varieties in tumor appearance and ambiguous tumor limits. Medical imaging field requests images with high determination and higher data substance for important infection finding and representation. Brain tumor segmentation expects to isolate the distinctive tumor tissues, for example, dynamic cells, necrotic center, and edema from ordinary brain tissues of White Matter (WM), Gray Matter (GM), Cerebrospinal Fluid (CSF), Hard tissue and Soft tissue. Combination of at least two images taken from various modalities delivers another one which contains more exact data on the scene than any of the individual source images. This strategy enhances the nature of information. Image fussion is one of the essential repreparing ventures in advanced digital image remaking. Medical imaging field requests images with high determination and higher data substance for essential ailment finding and perception without. The motivation behind this paper is to give an exhaustive review to MRI-based brain tumor segmentation strategies. A target appraisal about segmentation is introduced and future advancements and patterns are tended to for MRI-based brain tumor segmentation techniques.

Keywords:-CSF, XRA

I. INTRODUCTION

Tumor is an uncontrolled development of disease cells in any part of the body. Tumors are of various sorts and have distinctive qualities and diverse treatments. At present, brain tumors are named primary brain tumors and metastatic brain tumors. The previous start in the brain and tend to remain in the brain, the last start as a disease somewhere else in the body and spreading to the I groups brain tumors under the magnifying instrument. By and large, grade I and grade II are kind brain tumor (low-grade); Images are threatening brain tumor (high-grade). For the most part, if poor quality brain tumor is not treated, it is probably going to decay to high-review brain tumor. The 2012 CBTRUS (Central Brain Tumor Registry of the United States) Statistical Report has additionally demonstrated that brain tumors are the second driving reason for disease related passings in kids under age 20 and in guys ages 20-39 (leukemia is the first) and the fifth driving reason for malignancy related passing's in females ages 20-39. An expected 69 720 new instances of essential brain tumors were relied upon to be analyzed in 2013 and included both dangerous (24 620) and non-threatening (45 100) brain tumors. This gauge depends on an utilization of age-sex-race-particular rate rates from the 2013 CBTRUS Statistical Report utilizing SEER and NPCR information to extend 2013 US populace gauges for the respective age-sex-race gatherings (www.abta.org/aboutus/

news/brain-tumor- statistics/). Along these lines, brain tumors are genuinely jeopardizing individuals' lives and early revelation and treatment have turned into a need. In the clinical viewpoint, treatment alternatives for brain tumor incorporate surgery, radiation treatment or chemotherapy.

With headway in imaging innovation, diagnostic imaging has turned into a vital instrument today. Xray angiography (XRA), magnetic resonance angiography (MRA), magnetic resonance imaging (MRI), computed tomography (CT), and other imaging modalities are intensely utilized as a part of clinical practice. Such images give an integral data about a patient. Vein depiction on medicinal pictures frames a basic stride in tackling a few down to earth applications, for example, conclusion of the vessels (e.g. stenosis or distortions) and enlistment of patient images acquired at various circumstances. Segmentation calculations shape the quintessence of medical images applications, for example, radiological analytic frameworks, multimodal images registration, making anatomical atlas, perception, and computer aided surgery.

Segmentation techniques fluctuate contingent upon the image modality, application area, strategy will be programmed or self-loader, and other particular elements. There is no single segmentation strategy which can extricate vasculature from each medical image modality. While a portion of the strategies utilizes unadulterated intensity-based example acknowledgment systems, for example, thresholding took after by associated part examination, some different techniques apply unequivocal vessel models that extracts the vessel shape. In light of the image quality and the image antiquity, for example, noises, some segmentation plans may require image preprocessing before the segmentation calculation. Then again, a few strategies apply present preparing on beat the issues emerging from over segmentation.

II. LITERATURE REVIEW

Matthieu Lê[1], demonstrates a proof of idea for programmed arranging of customized the radiotherapy for brain tumors. A computational model of glioblastoma development is consolidated with an exponential cell survival model to portray the impact of radiotherapy. The model is customized to the magnetic resonance images (MRIs) of a given patient. It considers the vulnerability in the model parameters, together with the instability in the MRI segmentations. The registered likelihood dispersion over tumor cell densities, together with the cell survival model, is utilized to characterize the medicine measurement appropriation, which is the reason for ensuing Intensity Modulated Radiation Therapy (IMRT) arranging. Contingent upon the clinical information accessible, contrast three unique situations with customize the model.

First, to consider a single MRI acquisition before therapy, as it would frequently be the case in clinical routine. Second, to use two MRI acquisition at two different time points in order to personalize the model and plan radiotherapy. Third, to include the uncertainty in the segmentation process. The application of this approach on two patients diagnosed with high grade glioma. Introduce two methods to derive the radiotherapy prescription dose distribution, which are based on minimizing integral tumor cell survival using the maximum a posteriori or the expected tumor cell density. It show how this method allows the user to a patient particular radiotherapy compute scheduling conformal to the tumor penetration. In further present extensions of the method in order to neighboring organs spare at risk hv redistributing the dose. The presented approach and its proof of concept may help in the future to better target the tumor and spare organs at risk.

According to the three novel principled approaches to compute the prescription dose. First, minimize the surviving fraction of tumor cells after irradiation for the most probable tumor cell density. Second, minimize the expected survival fraction tumor cells after irradiation. Third, present an approach to correct the prescription dose to take into account the presence of adjacent organs at risk. A summary of the method is illustrated in Figure 1. To our knowledge, this is the first work that uses a personalized model of brain tumor growth taking into account the uncertainty in tumor growth parameters and the clinician's segmentations in order to optimize radiotherapy planning.



Fig. 1. Summary of the method: the segmentation of the tumor on the different MRIs is used to personalize the tumor growth model. This is combined with a dose response model to define the prescription dose. Finally, the delivered dose is optimized using 9 equally spaced coplanar photon beams. The color code indicates which data is used for the different scenarios: one or two MRI acquisition at two different time points, the clinical segmentations or plausible samples to take into account the segmentation uncertainty.

Here they used some methods for segmentation i.e., One time point is used to taking sample from the posterior distribution using the Metropolis-Hasting algorithm first described by [7], and used for tumor growth personalization in [8]. Two time points method is used by Gaussian Process Hamiltonian Monte Carlo (GPHMC) algorithm. The only difference is that at each iteration, taken randomly sample segmentations from the prior P(Zi). In Radiotherapy planning they used the methods MAP Dose, Probabilistic Dose and corrected Dose to finding tumor cell density.



Fig 2 Prescription MAP doses in Gray for the clinical plan and the three different personalized plans. From top to bottom: clinical plan, using only the second time point, using the two time points, using the two time points and the segmentation uncertainty. From left to right: axial, coronal, and sagittal views.

Figure 2 shows the prescription MAP doses in the three scenarios: i) using only the second time point, ii) using the two time points, iii) using the two time points and the segmentation uncertainty. In accordance with the histograms of invisibility index can see that the MAP dose using a single time point is more shallow compared to the doses using two time points (see the arrows on the different views of Figure 2).

Finally, by using IMRT Planning, optimize an Intensity Modulated Radiation Therapy (IMRT) plan using 9 equally spaced coplanar 6 MV photon beams and a piece-wise quadratic objective function, as detailed in [9], [10]. Dose-calculation is performed using the software CERR [11]. Here only used to compare the segmentation image of the brain tumor.

The segmentation is taken by only using the MRI. They didn't use different modalities for the segmentation. The inclusion of the fractionation scheme of the delivered dose could be optimized. It should be investigated if more conformal dose delivery techniques such as proton therapy lead to IMRT planning more conformal to the prescribed dose.

Sérgio Pereira[2], an automatic segmentation method based on Convolutional Neural Networks (CNN), exploring small 3 x 3 kernels. Also investigated the use of intensity normalization as a pre-processing step, which though not common in CNN-based segmentation methods, proved together with data augmentation to be very effective for brain tumor segmentation in MRI images. It was approved in the Brain Tumor Segmentation Challenge 2013 database (BRATS 2013), getting all the while the main position for the entire, center, and upgrading districts in Dice Similarity Coefficient metric (0.88, 0.83, 0.77) for the Challenge data set. Likewise, it acquired the general initially position by the online assessment stage. Participated in the on-site BRATS 2015 Challenge using the same model, obtaining the second place, with Dice Similarity Coefficient metric of 0.78, 0.65, and 0.75 for the complete, core, and enhancing regions, respectively. In brain tumor segmentation, it has several methods that explicitly develop a parametric or non-parametric probabilistic model for the underlying data.

In brain tumor segmentation, to find several methods that explicitly develop a parametric or non-parametric probabilistic model for the underlying data. These models usually include a likelihood function corresponding to the observations and a prior model. Being abnormalities, tumors can be segmented as outliers of normal tissue, subjected to shape and connectivity constrains [12]. Other approaches rely on probabilistic atlases [13]-[15]. In the case of brain tumors, the atlas must be estimated at segmentation time, because of the variable shape and location of the neoplasms [13]-[15]. Tumor growth models can be used as estimates of its mass effect, being useful to improve the atlases [14], [15]. The neighborhood of the voxels provides useful information for achieving smoother segmentations through Markov Random Fields (MRF) [12]. Zhao et al. [16] also used a MRF to segment brain tumors after a first over segmentation of the image into supervoxels, with a histogram-based estimation of the likelihood function. As observed by Menze et al. [16], generative models generalize well in unseen data, but it may be difficult to explicitly translate prior knowledge into an appropriate probabilistic model.

Here discussed with methodologies what used here. It starts by a pre-processing stage consisting of bias field correction, intensity and patch normalization. After that, during training, the number of training patches is artificially augmented by rotating the training patches, and using samples of High Grade Gliomas (HGG) to augment the number of rare Low Grade Gliomas (LGG) classes. The CNN is built over convolutional layers with small 3 x 3 kernels to allow deeper architectures. In this method, address the heterogeneity caused by multisite multi-scanner acquisitions of MRI images using intensity normalization as proposed by Nyúl *et al.* It shows that this is important in achieving a good segmentation. Brain tumors are highly variable in their spatial localization and structural composition, so it has investigated the use of data augmentation to cope with such variability.



Fig. 3 Examples of segmentations obtained with cross-validation, showing the effect of each component of the proposed method. In the first row, we have a HGG, and in the bottom row a LGG. Each color represents a tumor class: green-edema, blue-necrosis, yellow-non-enhancing tumor and red-enhancing tumor.

Referring to Figure 3, find that using ReLU as an activation function resulted in an excessive segmentation of non-enhancing and necrosis regions outside the core for HGG.

The draw back is used in hard and soft tissues. In edema portions the lesion parts are not concentrated much and not improved the segmentation acquiring percentage and also that was used for only MRI images not combining different modalities images.

Nicolas Cordier [3], describe a novel and generic approach to address fully-automatic segmentation of brain tumors by using multi-atlas patch-based voting techniques. In addition to avoiding the local search window assumption, the conventional patchbased framework is enhanced through several simple procedures: A probabilistic model automatically delineates regions of interest enclosing high-probability tumor volumes, which allows the algorithm to achieve highly competitive running time despite minimal processing power and resources.

This method was evaluated on Multimodal Brain Tumor Image Segmentation challenge datasets. State-of-the-art results are achieved, with a limited learning stage thus restricting the risk of overfit. Moreover, segmentation smoothness does not involve any post-processing. In paper [17] they didn't concentrate on edema portions. That will be carried out here, they did 1) Glioma Segmentation [18]–[20] by using machine learning algorithm is trained offline, 2) Multi-Atlas Segmentation: When applied to glioma segmentation, machine learning techniques are confronted with two major problems. First, the amount of training data is usually small: for instance, there are only 20 highgrade training cases for the 2013 BraTS benchmark [18]. Second, most algorithms require a computationally intensive offline learning stage, which can be subject to overfit. Multi-atlas segmentation methods are appealing as they can cope with a small training dataset, and are performed online, which allows a seamless integration of new cases into the training dataset. The methodologies what they used are the efficient segmentation process with automatically by using multi-atlas patch-based voting techniques.

But it not satisfies this might be due to the fact that this approach only considers distances between patches to perform the segmentation. This could lead to drastically different results for any application which would make use of the nearestneighbour per-se.

Bjoern H. Menze [4], generative probabilistic model for segmentation of brain lesions in multidimensional images that generalizes the EM segmenter, a common approach for modelling brain images using Gaussian mixtures and a probabilistic tissue atlas that utilizes expectation-maximization (EM), to gauge the mark delineate another image. In this model augments the probabilistic atlas of the healthy tissues with a latent atlas of the lesion. An estimation algorithm with closed-form EM update equations. The strategy removes an inert atlas earlier dispersion and the lesion posterior back appropriations mutually from the image information. It delineates lesion areas individually in each channel, allowing for differences in lesion appearance across modalities, an important feature of many brain tumor imaging sequences.

Here also propose discriminative model extensions to map the output of the generative model to arbitrary labels with semantic and biological meaning, such as "tumor core" or "fluid-filled structure", but without а one-to-one correspondence to the hypo- or hyper-intense lesion areas identified by the generative model. The generative model that has been intended for tumor lesions to sum up well to stroke images, and the broadened discriminative - discriminative model to be one of the top positioning techniques in the BRATS assessment.

Some methods have been developed for less frequent and less aggressive tumors [21]-[24]. Tumor segmentation methods often borrow ideas from other brain tissue and other brain lesion segmentation methods that have achieved a considerable accuracy [25]. Brain lesions resulting from traumatic brain injuries [26], [27] and stroke [28], [29] are similar to glioma lesions in terms of size and multimodal intensity patterns, but have attracted little attention so far. Discriminative probabilistic models directly learn the differences between the appearance of the lesion and other tissues from the data. Although they require substantial amounts of training data to be robust to artefacts and variations in intensity and shape, they have been applied successfully to tumor segmentation tasks [30]-[34]. Discriminative approaches proposed for tumor segmentation typically employ dense, voxel-wise features from anatomical maps [35] or image intensities, such as local intensity differences [36], [37] or intensity profiles, that are used as input to inference algorithms such as support vector machines [38], decision trees ensembles [35], [39], [40], or deep learning approaches [41], [42].

Methodology what used is a new generative probabilistic model for channel-specific tumor segmentation in multi-dimensional images. The model shares information about the spatial location of the lesion among channels while making full use of the highly specific multimodal, i.e., multivariate, signal of the healthy tissue classes for segmenting normal tissues in the brain. In expansion to the tissue sort, the model incorporates a latent variable for each voxel encoding the likelihood of watching a tumor at that voxel, like [43], [44]. The probabilistic model formalizes subjective biological knowledge about hyper- and hypo-intensities of lesion structures in different channels. Our approach extends the general EM segmentation algorithm [45], [46] using probabilistic tissue atlases [47], [48], [49] for situations when specific spatial structures cannot be described sufficiently through population priors.

The methodology which is not concentrated on integrating image segmentation with tumor growth models enforcing spatial or temporal relations as in [50], [51]. Tumor growth models—often described through partial differential equations [52] – offer a formal description of the lesion evolution, and could be used to describe the propagation of channel-specific tumor outlines in longitudinal series [53], as well as a shape and location prior for various tumor structures [54]. This could also promote a deeper integration of underlying functional models of disease progression and formation of image patterns in the modalities that are used to monitor this process [55].

Matthieu Lê [5], estimating the parameters of the reaction-diffusion model is difficult because of the lack of identifiability of the parameters, the uncertainty in the tumor segmentations, and the model approximation, which cannot perfectly capture the complex dynamics of the tumor evolution. It aims at analyzing the uncertainty in the patient specific parameters of a tumor growth model, by sampling from the posterior probability of the parameters knowing the magnetic resonance images of a given patient. The estimation of the posterior probability is based on: 1) a highly parallelized implementation of the reactiondiffusion equation using the Lattice Boltzmann Method (LBM), and 2) a high acceptance rate Monte Carlo technique called Gaussian Process Hamiltonian Monte Carlo (GPHMC). Compare this personalization approach with two commonly used methods based on the spherical asymptotic analysis of the reaction-diffusion model, and on a derivative-free optimization algorithm.

Demonstrate the performance of the method on synthetic data, and on seven patients with a glioblastoma, the most aggressive primary brain tumor. This Bayesian personalization produces more informative results. In particular, it provides samples from the regions of interest and highlights the presence of several modes for some patients. In previous approaches based contrast. on optimization strategies fail to reveal the presence of different modes, and correlation between parameters. The proposed Bayesian method for the personalization of a tumor growth model based on the re action diffusion equation. Proposed the use of the Lattice Boltzmann Method (LBM) to implement the tumor growth model which results in reduced computation times. This is combined with a high acceptance rate Monte Carlo technique called the Gaussian Process Hamiltonian Monte Carlo (GPHMC). Contrary to previous approaches, this method does not rely on approximations of the forward model (resp. posterior probability) using reduced order models [56], [57] (resp. sparse grid methods [58]). Compare that this approach to two methods adapted from the literature. The former is based on the spherical asymptotic analysis of the forward model, inspired by the work of Swanson et al. [59], [60]. The latter is based on the gradientfree optimization method BOBYQA, and is used in the work of Konukoglu et al. [61]. This paper extends [62] with a comparison with a spherical asymptotic analysis of the personalization, and more comprehensive analysis on 3 additional patients. Also, a new likelihood model based on the 95 th percentile of the Hausdorff distance is used, as well as a new log-uniform prior for the parameters of interest. Finally, the parameters of the GPHMC have been updated to increase the robustness of the personalization: i) the initialization of the Gaussian process is now done with a coarse grid to ensure that the whole space of parameters is covered, ii) the parameters of the Gaussian process are set by maximizing the likelihood, iii) the noise level of the likelihood model has been reduced from $\sigma = 10$ mm in [62] to $\sigma = 5$ mm in order to increase the focus on the region of interest (i.e., the posterior is more peaked when the noise level is lower).

In this paper draw back is intend to apply the Bayesian personalization in order to explicitly take into account the uncertainty in the expert's segmentation. More specifically, the segmentations used during each model evaluation could be sampled in the space of plausible segmentations [63]. Believe that this work could be used for automatic personalized therapy planning. Some work has already been done on relating tumor growth models to radiation response models to better define radiation therapy plans [64], [65], [66]. Such a method could provide personalized therapy plans taking into account the uncertainty in the model's parameters.

Fuyong Xing [6], Computer-aided image analysis of histopathology specimens could potentially provide support for early detection and improved characterization of diseases such as brain tumor. pancreatic (NET). neuroendocrine tumor Automated nucleus segmentation is a prerequisite for various quantitative analyses including automatic morphological feature computation. However, it stays to be a testing issue because of the brain boggling nature of histopathology images. Proposed a learning-based framework for robust and automatic nucleus segmentation with shape preservation. Given a nucleus image, it begins with a deep convolutional neural network (CNN) model to generate a probability map, on which an iterative region merging approach is performed for shape segmentation initializations. Next, a novel algorithm is abused to separate individual nuclei joining a strong selection-based sparse shape model and a neighborhood ghastly deformable model. One of the significant benefits of the proposed framework is that it is applicable to different staining histopathology images.

Due to the element learning normal for the profound CNN and the abnormal state shape earlier displaying, the proposed strategy is sufficiently general to perform well over various situations. The methodology used for tested the proposed algorithm on three large-scale pathology image datasets using a range of different tissue and stain preparations, and the comparative experiments with recent state of expressions of the human experience exhibit the unrivalled execution of the proposed approach. To join bottom-up and top-down information together to achieve nucleus delineation considering the fact that nucleus boundaries are often weak or even missing. In addition, the proposed algorithm can handle misleading cues due to inhomogeneous intensity or background clutter in the digitized specimens. Sparse shape model has shown to be more effective than PCA-based shape prior due to its insensitiveness to object occlusion [67], [68]. However, using all training shapes is inefficient during sparse reconstruction on a large dataset at run-time. KSVD [69] is a popular dictionary learning algorithm, but it is not designed as a discriminative and selection-based dictionary learning method with respect to classification and segmentation. Here, a novel and robust selectionbased dictionary learning algorithm for nucleus shape modelling is used.

Different from KSVD, this method directly selects the most representative nucleus shapes from the training dataset as dictionary bases. The robustness of the dictionary learning method is achieved by minimizing an integrated square error with a sparse constraint. In order to simultaneously and efficiently segment multiple nuclei, combine a topdown shape prior model and a bottom-up deformable model with locality and repulsion constraints. The proposed algorithm alternately performs shape deformation using the efficient local repulsive deformable model, and shape inference using the shape prior derived from the sparse shape model. The flowchart of nucleus segmentation is shown in Fig. 2.Modules are i) Selection-Based Sparse Shape Model, 2) Shape Deformation, given initial contours, the proposed segmentation framework alternately performs shape deformation with the repulsive active contour model and shape inference with sparse shape prior. The shapes always expand from inside nuclei, one nucleus, and evolve towards nucleus per boundaries. In the active contour model, contours move based on image appearance information until it reaches a stable state, where the associated energy function achieves a minimum value; in the shape inference stage, contours evolve based on high level shape prior to constrain the shapes. This alternative operation scheme of combing bottom-up and top-down information has been successfully applied to biomedical image segmentation [67], [68].

The draw back of this paper is considering that whole-slide scanned histopathological images are usually with very large sizes (e.g., 10000 10000), in future reduce the running time of this algorithm method using cloud computing techniques. By dividing the whole image into multiple partiallyoverlapped tiles and distributing them onto different workers, concurrent cell segmentation can be achieved using a master-worker manner in the Spark cloud computing platform [70]. Our future work is to implement the proposed method with cloud computing techniques so that it can be adaptive to large-scale images.

III. EVALUATION AND VALIDATION

The legitimacy of brain tumor segmentation is an essential issue in restorative image examination since it directly affects surgical arranging. Figuring the cover with the ground truth has turned into the most widely recognized approach to quantitatively assess segmentation comes about. A few years prior, a lion's share of analysts approved their calculations on a set number of cases from their own particular information because of the absence of brain tumor database with ground-truth segmentations that is accessible to a wide group of clinicians and specialists. Huge numbers of the present brain tumor segmentaion techniques work MRI images due to the non-intrusive and great soft tissue difference of MRI and utilize arrangement and grouping strategies by utilizing distinctive components and considering spatial data in a nearby neighborhood. The motivation behind these techniques is to give a preparatory judgment on analysis, tumor monitoring and treatment getting ready for the doctor.

This makes it hard to analyze the execution of various strategies against each other standard. Subsequently, the exactness, legitimacy, and vigor individual strategies of the can't be straightforwardly contrasted and each other in light of the fact that the diverse measurements were utilized. The current most prevalent open MRI database for a target correlation of brain tumor segmentation calculations. Tables 1 and 2 demonstrate some present open instruments and databases for brain tumor segmentation, individually.

IV. CONCLUSION

In this paper we have achieved a fractional overview of different segmentations for MRI brain image with sample data set. A near review is made on different systems. After assessment of understood strategy it is plainly demonstrated the different strategies which can segment the tumor image effectively and give exact outcome. This work will be stretched out for new calculation for brain tumor segmentation which will give more proficient outcome than the current techniques in not so distant future. Computational time will likewise be considered to look at this system proficiently. As the conclusion tumor is a confused and touchy errand, exactness and dependability are constantly doled out much significance. Hence an intricate strategy that high lights new vistas for growing more vigorous image segmentation system is much looked for.

REFERENCES

- Matthieu Lê et al., "Personalized Radiotherapy Planning Based on a Computational Tumor Growth Model", in IEEE Transactions On Medical Imaging, VOL. 36, NO. 3, 2017.
- [2] Sérgio Pereira et al., Brain Tumor Segmentation Using Convolutional Neural Networks in MRI Images, IEEE Transactions On Medical Imaging, VOL. 35, NO. 5, 2016
- [3] Nicolas Cordier et al., "A Patch-Based Approach for the Segmentation of Pathologies: Application to Glioma Labelling", IEEE Transactions On Medical Imaging, VOL. 35, NO. 4, 2016.
- [4] Bjoern H. Menze et al., "A Generative Probabilistic Model and DiscriminativeExtensions for Brain Lesion Segmentation—With Application to Tumor and Stroke" IEEE Transactions On Medical Imaging, VOL. 35, NO. 4, 2016.
- [5] Matthieu Lê et al., "MRI Based Bayesian Personalization of a Tumor Growth Model", IEEE Transactions On Medical Imaging, VOL. 35, NO. 10, 2016.
- [6] Fuyong Xing et al., "An Automatic Learning-Based Framework for Robust Nucleus Segmentation", IEEE Transactions On Medical Imaging, VOL. 35, NO. 2, 2016
- [7] C. E. Rasmussen, "Gaussian processes to speed up hybrid Monte Carlo for expensive Bayesian integrals," Bayesian Statist., vol. 7, pp. 651– 659, 2003.
- [8] M. Lê et al., "Bayesian personalization of brain tumor growth model," in Proc. Int. Conf. Med. Image Comput. Comput. Assist. Intervent., 2015, pp. 424–432.
- [9] J. Unkelbach, B. H. Menze, E. Konukoglu, F. Dittmann, N. Ayache, and H. A. Shih, "Radiotherapy planning for glioblastoma based on a tumor growth model: Implications for spatial dose redistribution," *Phys. Med. Biol.*, vol. 59, no. 3, p. 771, 2014.

- [10] J. Unkelbach *et al.*, "Radiotherapy planning for glioblastoma based on a tumor growth model: Improving target volume delineation," *Phys. Med. Biol.*, vol. 59, no. 3, p. 747, 2014.
- [11] J. O. Deasy, A. I. Blanco, and V. H. Clark, "CERR: A computational environment for radiotherapy research," *Med. Phys.*, vol. 30, no. 5, pp. 979–985, 2003.
- [12] M. Prastawa *et al.*, "A brain tumor segmentation framework based on outlier detection," *Med. Image Anal.*, vol. 8, no. 3, pp. 275–283, 2004.
- [13] B. H. Menze et al., "A generative model for brain tumor segmentation in multi-modal images," in *Medical Image Computing and Comput.- Assisted Intervention-MICCAI 2010*. New York: Springer, 2010, pp. 151–159.
- [14] A. Gooya *et al.*, "GLISTR: Glioma image segmentation and registration," *IEEE Trans. Med. Imag.*, vol. 31, no. 10, pp. 1941–1954, Oct. 2012.
- [15] D. Kwon *et al.*, "Combining generative models for multifocal glioma segmentation and registration," in *Medical Image Computing and Comput.-Assisted Intervention-MICCAI* 2014. New York: Springer, 2014, pp. 763–770.
- [16] B. Menze *et al.*, "The multimodal brain tumor image segmentation benchmark (BRATS)," *IEEE Trans. Med. Imag.*, vol. 34, no. 10, pp. 1993–2024, Oct. 2015.
- [17] P. Y. Wen *et al.*, "Updated response assessment criteria for high-grade gliomas: Response assessment in neuro-oncology working group," *J. Clin. Oncol.*, vol. 28, no. 11, pp. 1963–1972, 2010.
- [18] B. Menze *et al.*, "The multimodal brain tumor image segmentation benchmark (BraTS)," *IEEE Trans. Med. Imag.*, vol. 34, no. 10, pp. 1993–2024, Oct. 2015.
- [19] D. Zikic *et al.*, "Decision forests for tissuespecific segmentation of high-grade gliomas in multi-channel MR," in *MICCAI 2012*. New York: Springer, 2012, pp. 369–376.
- [20] N. J. Tustison *et al.*, "Optimal symmetric multimodal templates and concatenated random forests for supervised brain tumor segmentation (simplified) with ANTsR," *Neuroinformatics*, pp. 1–17, 2014.
- [21] M. Kaus *et al.*, "Segmentation of meningiomas and low grade gliomas in MRI," in *Proc. MICCAI*, 1999, pp. 1–10.

- [22] Y.-F. Tsai, I.-J. Chiang, Y.-C. Lee, C.-C. Liao, and K.-L. Wang, "Automatic MRI meningioma segmentation using estimation maximization," *Proc. IEEE Eng. Med. Biol. Soc.*, vol. 3, pp. 3074–3077, 2005.
- [23] E. Konukoglu *et al.*, "Monitoring slowly evolving tumors," *Proc. ISBI*, pp. 1–4, 2008.
- [24] B. Bach Cuadra, C. Pollo, A. O. Bardera, O. Cuisenaire, and J. P. Thiran, "Atlas-based segmentation of pathological brain MR images using a model of lesion growth," *IEEE Trans. Med. Imag.*, vol. 23, no. 10, pp. 1301–14, Oct. 2004.
- [25] M. Styner and , "3D segmentation in the clinic: A grand challenge II: MS lesion segmentation," *MIDAS J.*, pp. 1–5, 2008.
- [26] A. Irimia *et al.*, "Comparison of acute and chronic traumatic brain injury using semiautomatic multimodal segmentation of MR volumes," *J. Neurotrauma*, vol. 28, pp. 2287– 2306, 2011.
- [27] M. Shenton *et al.*, "A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury," *Brain Imag. Behav.*, vol. 6, pp. 137– 192, 2012.
- [28] T. D. Farr and S. Wegener, "Use of magnetic resonance imaging to predict outcome after stroke: A review of experimental and clinical evidence," *J. Cerebr Blood Flow Metab.*, vol. 30, pp. 703–717, 2010.
- [29] I. Rekik, S. Allassonnière, T. K. Carpenter, and J. M. Wardlaw, "Medical image analysis methods in MR/CT-imaged acute-subacute ischemic stroke lesion: Segmentation, prediction and insights into dynamic evolution simulation models. A critical appraisal," *NeuroImage: Clinical*, 2012.
- [30] D. Cobzas, N. Birkbeck, M. Schmidt, M. Jagersand, and A. Murtha, "3D variational brain tumor segmentation using a high dimensional feature set," in *Proc. ICCV*, 2007, pp. 1–8.
- [31] A. Lefohn, J. Cates, and R. Whitaker, "Interactive, GPU-based level sets for 3D brain tumor segmentation," in *Proc. MICCAI*, 2003, pp. 564–572.
- [32] L. Gorlitz, B. H. Menze, M.-A. Weber, B. M. Kelm, and F. A. Hamprecht, "Semi-supervised tumor detection in magnetic resonance spectroscopic images using discriminative

random fields," in *Proc DAGM*. New York: Springer, 2007, LNCS, pp. 224–233.

- [33] C. Lee, S. Wang, A. Murtha, and R. Greiner, "Segmenting brain tumors using pseudo conditional random fields," in *Proc MICCAI*. New York: Springer, 2008, vol. 5242, LNCS, pp. 359–366.
- [34] M. Wels, G. Carneiro, A. Aplas, M. Huber, J. Hornegger, and D. Comaniciu, "A discriminative model-constrained graph cuts approach to fully automated pediatric brain tumor segmentation in 3D MRI," in *Proc MICCAI*. New York: Springer, vol. 5241, LNCS, pp. 67–75.
- [35] D. Zikic, B. Glocker, E. Konukoglu, A. Criminisi, C. Demiralp, J. Shotton, O. M. Thomas, T. Das, R. Jena, and S. J. Park, "Decision forests for tissue-specific segmentation of high-grade gliomas in multichannel MR," in *Proc. MICCAI*, 2012.
- [36] E. Geremia *et al.*, "Spatial decision forests for MS lesion segmentation in multi-channel magnetic resonance images," *Neuroimage*, vol. 57, pp. 378–90, 2011.
- [37] E. Geremia, B. H. Menze, and N. Ayache, "Spatially adaptive random forests," in *Proc.* 2013 IEEE 10th Int. Symp. Biomed. Imag., 2013, pp. 1344–1347.
- [38] S. Bauer *et al.*, "Multi-scale modeling for image analysis of brain tumor studies," *IEEE Trans. Bio-Med. Eng.*, vol. 59, no. 1, pp. 25– 29, Jan. 2012.
- [39] W. Wu, A. Y. Chen, L. Zhao, and J. J. Corso, "Brain tumor detection and segmentation in a conditional random fields framework with pixelpairwise affinity and superpixel-level features," *Int. J. Comput. Assist. Radiol. Surg.*, pp. 1–13, 2013.
- [40] N. J. Tustison *et al.*, "Optimal symmetric multimodal templates and concatenated random forests for supervised brain tumor segmentation (simplified) with ANTSR," *Neuroinformatics* vol. 13, no. 2, pp. 209–225, Apr. 2015.
- [41] P. Dvorak and B. H. Menze, "Structured prediction with convolutional neural networks for multimodal brain tumor segmentation," in *Proc MICCAI Med. Comput. Vis. Workshop*, 2015.
- [42] G. Urban, M. Bendszus, F. A. Hamprecht, and J. Kleesiek, "Multimodal brain tumor segmentation using deep convolutional neural

networks," in *Proc. MICCAI BRATS*, 2014, pp. 31–35.

- [43] T. Riklin-Raviv *et al.*, "Joint segmentation via patient-specific latent anatomy model," in *Proc MICCAI-PMMIA*, 2009, pp. 244–255.
- [44] T. Riklin-Raviv, K. Van Leemput, B. H. Menze, W. M. Wells, and P. Golland, "Segmentation of image ensembles via latent atlases," *Med.Image Anal.*, vol. 14, pp. 654– 665, 2010.
- [45] W. Wells, W. Grimson, R. Kikinis, and F. Jolesz, "Adaptive segmentation of MRI data," in *Proc Comput. Vis. Virtual Reality Robot. Med.*, 1995, pp. 57–69.
- [46] W. M. Wells, W. E. L. Grimson, R. Kikinis, and F. A. Jolesz, "Adaptive segmentation of MRI data," *IEEE Trans.Med. Imag.*, vol. 15, no. 4, pp. 429–442, 1996.
- [47] J. Ashburner and K. Friston, "Multimodal image coregistration and partitioning—A unified framework," *Neuroimage* vol. 6, no. 3, pp. 209–217, Oct. 1997.
- [48] K. Van Leemput, F. Maes, D. Vandermeulen, and P. Suetens, "Automated model-based bias field correction of MR images of the brain," *IEEE Trans. Med. Imag.*, vol. 18, no. 10, pp. 885–896, Oct. 1999.
- [49] K. M. Pohl, J. Fisher, W. Grimson, R. Kikinis, and W. Wells, "A Bayesian model for joint segmentation and registration," *Neuroimage*, vol. 31, pp. 228–239, 2006.
- [50] Y. Tarabalka, G. Charpiat, L. Brucker, and B. H. Menze, "Spatio-temporal video segmentation with shape growth or shrinkage constraint," *IEEE Trans. Image Process.*, vol. 23, no. 9, pp. 3829–3840, Sep. 2014.
- [51] E. Alberts, G. Charpiat, Y. Tarabalka, M. A. Weber, C. Zimmer, and M.B. H. Youdim, "A nonparametric growth model for estimating tumor growth in longitudinal image sequences," in *Proc MICCAI Brain Lesions Workshop (BrainLes).* New York: Springer, 2015, LNCS.
- [52] B. H. Menze, E. Stretton, E. Konukoglu, and N. Ayache, "Image-based modeling of tumor growth in patients with glioma," in *Optimal Control in Image Processing*, C. S. Garbe, R. Rannacher, U. Platt, and T. Wagner, Eds. Heidelberg, Germany: Springer, 2011.
- [53] E. Konukoglu *et al.*, "Image guided personalization of reaction-diffusion type tumor growth models using modified

anisotropic eikonal equations," *IEEE Trans. Med. Imag.*, vol. 29, no. 1, pp. 77–95, Jan. 2010.

- [54] A. Gooya *et al.*, "GLISTR: Glioma image segmentation and registration," *IEEE Trans. Med. Imag.*, vol. 31, no. 10, pp. 1941–1954, Oct.2012.
- [55] B. H. Menze *et al.*, "A generative approach for image-based modeling of tumor growth," in *Proc. IPMI*, 2011.
- [56] E. Konukoglu et al., "Efficient probabilistic model personalization integrating uncertainty on data and parameters: Application to eikonaldiffusion models in cardiac electrophysiology," Progr. Biophys. Molecular Biol., vol. 107, no. 1, pp. 134–146, 2011.
- [57] D. Neumann et al., "Robust image-based estimation of cardiac tissue parameters and their uncertainty from noisy data," in MICCAI. New York: Springer, 2014, pp. 9–16.
- [58] B. H. Menze, K. Van Leemput, A. Honkela, E. Konukoglu, M.-A. Weber, N. Ayache, and P. Golland, "A generative approach for imagebased modeling of tumor growth," in IPMI. New York: Springer, 2011, pp. 735–747.
- [59] H. L. Harpold, E. C. Alvord Jr, and K. R. Swanson, "The evolution of mathematical modeling of glioma proliferation and invasion," J. Neuropathol. Exp. Neurol., vol. 66, no. 1, 2007.
- [60] D. Corwin et al., "Toward patient-specific, biologically optimized radiation therapy plans for the treatment of glioblastoma," PloS One, vol. 8, no. 11, p. P. e79115, 2013.
- [61] E. Konukoglu et al., "Image guided personalization of reaction-diffusion type tumor growth models using modified anisotropic eikonal equations," IEEE Trans. Med. Imag., vol. 29, no. 1, pp. 77–95, Jan. 2010.
- [62] M. Lê, H. Delingette, J. Kalpathy-Cramer, E. Gerstner, T. Batchelor, J. Unkelbach, and N. Ayache, "Bayesian personalization of brain tumor growth model," in MICCAI. New York: Springer, 2015.
- [63] M. Lê, J. Unkelbach, N. Ayache, and H. Delingette, "GPSSI: Gaussian process for sampling segmentations of images," in MICCAI. New York: Springer, 2015.
- [64] J. Unkelbach et al., "Radiotherapy planning for glioblastoma based on a tumor growth

model: Improving target volume delineation," Phys. Med. Biol., vol. 59, no. 3, p. 747, 2014.

- [65] J. Unkelbach et al., "Radiotherapy planning for glioblastoma based on a tumor growth model: Implications for spatial dose redistribution," Phys. Med. Biol., vol. 59, no. 3, p. 771, 2014.
- [66] R. Rockne, E. AlvordJr., J. Rockhill, and K. Swanson, "A mathematical model for brain tumor response to radiation therapy," J. Math. Biol., vol. 58, no. 4-5, pp. 561–578, 2009.
- [67] S. Zhang, Y. Zhan, M. Dewan, J. Huang, D. N. Metaxas, and X. S. Zhou, "Deformable segmentation via sparse shape representation," in *Int. Conf. Med. Image Comput. Comput. Assist. Intervent. (MICCAI)*, 2011, pp. 451– 458.
- [68] S. Zhang, Y. Zhan, and D. N. Metaxas, "Deformable segmentation via sparse shape representation and dictionary learning," *Med. Image Anal.*, vol. 16, no. 7, pp. 1385–1396, 2012.
- [69] M. Aharon, M. Elad, and A. Bruckstein, "K-SVD: An algorithm for designing overcomplete dictionaries for sparse representation," *IEEE Trans. Signal Process.*, vol. 54, no. 11, pp. 4311–4322, Nov. 2006.
- [70] M. Sapkota, F. Xing, F. Liu, and L. Yang, "Skeletal muscle cell segmentation using distributed convolutional neural network," in *High Performance Comput. (HPC) Workshop Int. Conf. Med. Image Comput. Comput. Assist. Intervent. (MICCAI)*, 2015.