Personalized Radiotherapy Planning Based on a Computational Tumor Growth Model

Ramya.P¹, Karthika.A.R², Valli Suseela.R³, D.Ramalingam⁴

 ¹PG scholar, Department of Electronics and Communication Engineering, James college of Engineering and Technology, Nagercoil, (India)
²Assistant professor, Department of Electronics and Communication Engineering ,James college of Engineering and Technology, Nagercoil, (India)
³Assistant professor, Department of Electronics and Communication Engineering ,James college of Engineering and Technology, Nagercoil, (India)
⁴Principal, James college of Engineering and Technology, Nagercoil, (India)

ABSTRACT

Brain tumor segmentation is a critical strategy for early tumor determination and radiotherapy arranging. Proof of concept for the automatic planning of personalized radiotherapy for brain tumors. Computational models of glioblastoma grow this combined with an exponential cell survival model to describe the effect of radiotherapy. Depending on the clinical data available, we compare three different scenarios to personalize the model. First, we consider a single MRI acquisition before therapy, as it would usually be the case in clinical routine. Second, we use two MRI acquisitions at two distinct time points in order to personalize the model and plan radiotherapy. Third, we include the uncertainty in the segmentation process. To present the application of our approach on two patients diagnosed with high grade glioma. I 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. Further present Extensions of the method in order to spare adjacent organs a trisk by re-distributing 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

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 segmentation part is difficult because the region of interest appearance gets more varied and also has irregular boundaries. In classification task, the difficulty is that it is complex to differentiate the brain image into normal, abnormal and the type of abnormality. The techniques involved in image processing and the general concepts of brain tumor characterization based on magnetic resonance image (MRI) and describe its relevance for the diagnosis of different types of brain tumors. The section provides information about image processing, brain and brain

tumors, focus on potential of magnetic resonance (MR) for brain tumor diagnosis followed by problem statement, motivation and an overview of the thesis organization. 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. X- ray 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 frameworks, multimodal images registration, making anatomical atlas, perception, and computer analytic 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 unadulterated intensity-based example acknowledgment utilizes 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 the programmed arranging of customized 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 acquisitions 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 compute a patient particular radiotherapy scheduling conformal to the tumor penetration. In further present

xtensions of the method in order to spare neighboring organs at risk by 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.



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.

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 .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 SimilarityCoefficient 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 3kernels to allow deeper architectures. In this method, address the heterogeneity caused by multi-site 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. 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 patch- based 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-theart 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.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 a 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].

III. PROPOSED METHOD

Medical Imaging is witnessed to select the set of techniques that discreetly produce images of the internal part of the body. MRI (Magnetic resonance Imaging) brain tumor segmentation is a complicated task due to the variance and intricacy of tumors. Computer aided detection of abnormality in medical images is primarily

motivated by the necessity of achieving maximum possible accuracy. In general segmentation of images holds an important position in the area of image processing. For Segmentation process, k means clustering is used. The features are extracted from the tumor segmented region using Rough set theory. There are lots of methods for automatic and semi automatic image classification; most of them fail because of unknown noise, poor image contrast, in homogeneity and boundaries that are usual in medical images. Hence to make classification task for efficient, Support Vector Machine (SVM) and Feed Forward Neural Network (FFNN) is used to perform two major tasks. The first is to differentiate between normal and abnormal. The second function is to classify the type of abnormality is benign or malignant tumor. The results are tabulated for different classifiers and the proposed method result obtained is more accurate and reliable.

Medical imaging is a method and process to generate images of human body for doing many clinical progresses such as medical procedures seeking to reveal, examine or diagnose a particular disease. To create images of human body, medical imaging has many techniques like Computed Tomography (CT), XRAY, Ultrasound and Magnetic Resonance Imaging (MRI). X RAY which was invented by Winhelm in 1895 is considered to be the oldest source of electromagnetic radiation used for imaging, having wavelength in the range of 0.01 to 10 nanometres. To show the tumors which are located behind the bones of the skull or spine, for diagnosis, MRI is used. To cure Cancer is being a major goal of medical researchers for decades, but development of new treatments takes time consuming and also quiet expensive.

Scientific technologies may yet find the root causes of all cancers and develop safer methods for shutting them down but still some brain tumors are Benign (cancerous) and they need to be diagnosed before they grow or spread. Approximately 40 percent of all tumors are successfully treated with surgery and in some other cases with radiation. The number of malignant brain tumors appears to be increasing, but no clear reason has been yet found. Brain cancer is a complex disease which is classified into 120 different types. Benign tumors are life threatening as malignant tumors as they squeeze out normal brain tissue and disrupt function.

For clinical diagnosis, accurate classification of medical images is needed since it contains many complicated structures. Brain image classification is very important for detecting tumors. Magnetic resonance imaging (MRI) is a major imaging technique to detect abnormal changes in different parts of the brain in the beginning stage. MRI images have good contrast in comparison to computerized tomography (CT). The manual interpretation of brain tumor slices based on visual examination by physician may lead to missing diagnosis and time consuming when a large number of MRI brain images are analysed. To avoid human based diagnostic error, Computer Aided Diagnosis system is needed. For perfect classification of Brain tumors it is very essential to do Segmentation process and feature extraction.

A. METHODOLOGY

The fig .3 describes the block diagram of tumor detection and classification:

1. Input MRI Brain images are given from the Brain database.

- 2. The image obtained with the removal of noise is then segmented by means of K means clustering to extract the tumor in brain.
- 3. Feature extraction is done to the segmented part which contains the tumor by Rough Set theory.



Fig.3: Proposed work Methodology

B. MRI BRAIN IMAGE

MRI Image Data set is a collection of digitized images stored for research in Medical Image Processing. The input given is a Magnetic Resonance (MR) image which is taken from the data set. For our proposed brain tumor detection, MRI image dataset is utilized from many sources which are available in public. This image dataset contains 20 brain MRI images in which 10 brain images with tumor and the other 10 brain images without tumor.

The Brain image dataset are divided into two sets such as, (1) Training dataset (2) Testing dataset. For segmentation of brain tumor images, training data set is used whereas to check the performance of the proposed methodology, testing dataset is used. In this, the 15 images are utilized for the training purpose and the remaining 5 images are utilized for testing purpose. The figure which is given above shows some of the sample MRI images with tumor images and non tumor images.

Fig: 4 MRI Brain Image Dataset

C. PRE-PROCESSING

Pre-processing is an technique to improve the image data which removes the unwanted distortions or noise and enhances the image features which helps in further processing of image. Pre processing operations includes skull stripping, intensity normalization, contrast enhancement, de noising etc, which have a great impact on the results of segmentation of brain tumors. If the image has low contrast and quality, process would become very tedious and inaccurate which also affects the quality of the segmentation process. The presence of noise is common in all unprocessed medical images. One of the standard Pre processing steps in MRI images is Image de noising. To precisely outline the regions of interest between the normal brain tissues and brain tumor, `it is obvious that the noise components present in the MRI images should be removed and suppressed to the maximum possible extend to obtain accurate results after processing. In modern literature there are several techniques available for noise removal in images and enhance the contrast between the regions. One such technique is the use of pre processing filters. Here Gaussian filter is used for noise removal.

D.GAUSSIAN FILTER

The impulse response of a Gaussian filter is a Gaussian function. Gaussian filter is introduced to create an overshoot in the input step function during the decrease of rise and fall time. Hence Gaussian filter has minimum possible delay. It is also said that the input signal can be changed by Gaussian filter by convoluting it with a Gaussian function and this change in mathematically is said to be Weierstrass transform. Using Gaussian smoothing filter, the input image can be smoothed in order to reduce noise level.

F.SEGMENTATION OF TUMOR AFFECTED REGION

K means clustering is an algorithm applicable for unsupervised learning for clusters. Clustering is defined as the process of arranging the pixels based on some features. It is a pixel based method because of its simplicity, efficient and low computational complexity when compared other region based or edge based methods. It is suitable for biomedical image segmentation since the number of clusters is known for appropriate regions of

human anatomy. Hence identification of object is good in image segmentation by k means. Image segmentation is the technique to divide an image into many numbers of parts. In this process it makes use of saturation value of the pixel in order to determine that the intensity or hue of the pixel is present very nearer to human perception of the color in which the pixel represents.

The aim of clustering is to identify natural groupings of data from a large data set to provide a concise illustration of a system's behavior. K means clustering is a methodology of vector quantization, originally from signal processing, that is common for cluster analysis in data mining. K-means clustering aims to partition n observations into k clusters among which each observation belongs to the cluster with the closest mean, serving as a model of the cluster. This finishes up during a partitioning of the data space into Voronoi cells.

The algorithmic rule includes a loose relationship to the k nearest neighbor classifier, a standard machine learning technique for classification that is often confused with k means because of the k among the name. One can apply the 1nearest neighbor classifier on the cluster centers obtained by k means to classify new data into the prevailing clusters. This is referred to as nearest centroid classifier or Rocchio algorithm.

In K means algorithm, the number of clusters is defined. Then cluster centers are chosen randomly. The distance between every pixel to the centroid is computed. The distance between is of simple Euclidean function. Using the distance or gap formula the centre of the clusters is compared to single or many pixels. The pixel is then moved to the particular cluster space which has the shortest orbit among everything.

G. CLASSIFICATION BASED ON SUPPORT VECTOR MACHINE

Support Vector Machine (SVM) is a technique for the task of classification. The Support Vector Machine classifier is used to classify the image as tumor or not. In 1995, Support Vector Machine (SVM) has been developed, which is an effective supervised classifier and accurate learning technique. It is derived from the statistical theory invented by Vapnick in 1982. It produces successful classification results in several application domains, for e.g. medical diagnosis. From the statistical learning theory, SVM follows a structural risk minimization principle. Its kernel is to control the practical risk and classification capacity in order to broaden the margin between the classes and reduce the true costs. A support vector machine searches an optimal separating hyper-plane between members and non-members of a given class in a high dimension feature space.



Fig.5: Schematic Diagram of MRI Image Recognizer

H.TUMOR CLASSIFICATION BASED ON FEED FORWARD NEURAL NETWORK

The artificial neural network has three layers namely input layer, hidden layer and finally output layer. In order to select the parameter for training, input layer is used and it assumes the values from highest order. When the process is completed in the input layer it is further moved to the middle layer which is the hidden layer. Based on the validation data, the value of the hidden range can be altered. After the completion of process in hidden layer, the process is shifted to the output layer. Using the training data, the weights which are present in the hidden layer can be tested. Hence by using training data, the weight of the hidden layer has to be varied to give best variety of the hidden nodes. This is done to avoid under fitting or over fitting the information. The input and hidden layers are linked by synaptic links which is known as weights and similarly the hidden and output layer also have connection weights. If more than one hidden layer is present then the weight also exist between such layers. Then neural network also uses learning rule in which the error occur between the neural network and the output can be minimized by determining the connection weights.

The inputs to SVM algorithm and FFNT algorithm are the feature subset selected via multi texton technique. In our technique, the brain has been classified into two classes: normal and abnormal brain. In the classification procedure, abnormal brain is divided into malignant and benign tumors and is defined by vector. There are several common kernel functions namely,

$\exp\left[\frac{-\|\mathbf{y}_{i}-\mathbf{y}_{j}\|^{2}}{2\sigma^{2}}\right]$

3. Radial basis function : N

Among these kernel functions, RBF is proved to be effective, due to the fact that vectors are nonlinearly mapped to a very high dimension feature space. The optimal values of constants η and V are computed, where, η is the width of the kernel function and is the error/trade off parameter, which adjusts the importance of the separation error in the creation of the separation surface.

III. EVALUATIO AND VALIDATION

To prove the theoretical and practical construction, in this section the results for the proposed system is implemented and compared by using MRI brain images using MATLAB R2013a. MATLAB is used widely in many applications which have built in library functions with more toolbox. It is a very popular multipurpose numeric programming language which is meant for numerical computation as well as visualization. The final outcome of this work is a stable version of MATLAB based application to visually demonstrate the detection of brain tumor.

The MRI brain tumor classification process is an essential stage to analyse medical images because it has direct contact for further process like surgical planning, diagnosis, etc. The MRI dataset is taken from publicly available sources with 20 brain images in which 10 images with tumor and 10 images without tumor. Some of the sample MRI image dataset with and without tumor is shown in Figure 1. The application has been verified with different brain MRI and for displaying the results; three MR brain images (normal, benign tumor, malignant tumor) have been taken and processed for pre processing, segmentation, feature extraction and finally classification.

During the first stage, pre processing is done in which unwanted distortions or noise are removed using Gaussian filtering, the image features are enhanced and edge detection is done to map the boundary of the MRI image. In the second stage segmentation process is applied by k means clustering technique to arrange the pixels based on some features. In the third stage feature extraction is done by rough set theory which is done by step by step process based on the texture features.

A. MRI Input brain image:

It describes the MRI input brain image of normal and pathological brain conditions pose challenge from



technological

Fig.6 MRI Input brain image

In this method Segmentation process is done .Here input image is taken for pre-processing and k-means clustering.

Fig.7 Segmentation of MRI images

B. MRI malignant tumor brain image:

Fig.8 MRI Input brain image Malignant tumor

The fourth stage is final proposed stage (testing phase) meant for detection and classification of brain image as tumor or normal image. This stage is done by using two classifiers namely support vector machine (SVM) and feed forward neural network (FFNN) and the results which are obtained are verified through evaluation metrics such as sensitivity, specificity and accuracy.

Sensitivity=TP/(TP + FN)	.4
Specificity=TN/(TN + FP)	5
Accuracy= $(TN + TP)/(TN + TP + FN + FP)$	6

where TP is True Positive, TN is True Negative, FN is False Negative and FP is False Positive.

Fig.9 Segmentation of malignant tumor MRI images

a)Sensitivity: It is defined as the proportion of TP which can be correctly identified during diagnosis test. It also shows the ability of the test in detecting the normal (negative) condition.

b)Specificity: It is defined as the proportion of TN which can be correctly identified during diagnosis test. It also shows the ability of the test in detecting the disease.

c)Accuracy: It is defined as the proportion of true results which is true positive or true negative. Hence it measures the degree of veracity of a diagnostic test on a condition The fig.10 describes the detection of tumor

Fig.10 Detection of tumor

The result of the proposed method is compared with classification and detection process using support vector machine (SVM) and feed forward neural network (FFNN) classifiers. The testing results shows that better results have been obtained while using support vector machine (SVM) for brain tumor detection and classification.

Fig.11FeatureExtraction

Fig.12Adaboost classifier

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 innot 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

[1] J. Murray, Mathematical biology. Springer, 2002, vol. 2.

- [2] P. Tracqui, G. Cruywage, D. Woodward, G. Bartoo, J. Murray, and E. Alvord, "A mathematical model of glioma growth: the effect of chemotherapy on spatio temporal growth," Cell proliferation, vol. 28,no. 1, pp. 17–31, 1995.
- [3] R. Rockne, E. Alvord Jr, J. Rockhill, and K. Swanson, "A mathematicalmodel for brain tumor response to radiation therapy," Journal of mathematical biology, vol. 58, no. 4-5, pp. 561–578, 2009.
- [4] K. Swanson, E. Alvord, and J. Murray, "Virtual resection of gliomas : effect of extent of resection on recurrence," Mathematical and Computer Modelling, vol. 37, no. 11, pp. 1177–1190, 2003.

- [5] E. Stretton, E. Mandonnet, E. Geremia, B. H. Menze, H. Delingette, and N. Ayache, "Predicting the location of glioma recurrence after a resection surgery," in Proceedings of 2nd International MICCAI Workshop on Spatiotemporal Image Analysis for Longitudinal and Time-Series ImageData (STIA'12), ser. LNCS. Nice: Springer, October 2012.
- [6] O. Saut, J.-B. Lagaert, T. Colin, and H. M. Fathallah-Shaykh, "Amultilayer grow-or-go model for gbm: effects of invasive cells and anti-angiogenesis on growth," Bulletin of mathematical biology, vol. 76,no. 9, pp. 2306–2333, 2014.
- [7] E. Scribner, O. Saut, P. Province, A. Bag, T. Colin, and H. M.Fathallah-Shaykh, "Effects of antiangiogenesis on glioblastoma growth and migration: model to clinical predictions," PloS one, vol. 9, no. 12,p. e115018, 2014.
- [8] F. Raman, E. Scribner, O. Saut, C. Wenger, T. Colin, and H. M.Fathallah-Shaykh, "Computational trials: Unraveling motility phenotypes, progression patterns, and treatment options for glioblastomamultiforme," PloS one, vol. 11, no. 1, 2016.
- [9] K. Kristiansen, S. Hagen, T. Kollevold, A. Torvik, I. Holme, M. Stat, R. Nesbakken, R. Hatlevoll, M. Lindgren, A. Brun et al., "Combinedmodality therapy of operatedastrocytomas grade III and IV. Confirmation of the value of postoperativeirradiation and lack of potentiation of bleomycin on survival time: a prospective multicenter trial of the Scandinavian Glioblastoma Study Group," Cancer, vol. 47, no. 4, pp.649–652, 1981.
- [10] I. J. Barani and D. A. Larson, "Radiation therapy of glioblastoma," in Current Understanding and Treatment of Gliomas. Springer, 2015, pp.49–73.
- [11] W. Mason, R. Del Maestro, D. Eisenstat, P. Forsyth, D. Fulton, N. Laperri`ere, D. Macdonald, J. Perry, B. Thiessen, C. G. R. Committeeet al., "Canadian recommendations for the treatment of glioblastomamultiforme," Current Oncology, vol. 14, no. 3, p. 110, 2007.
- [12] D. Corwin, C. Holdsworth, R. C. Rockne, A. D. Trister, M. M. Mrugala, J. K. Rockhill, R. D. Stewart, M. Phillips, and K. R. Swanson, "Towardpatient-specific, biologically optimized radiation therapy plans for the treatment of glioblastoma," PLOS ONE, 2013.
- [13] C. Holdsworth, D. Corwin, R. Stewart, R. Rockne, A. Trister, K. Swanson, and M. Phillips, "Adaptive IMRT using a multi objective evolution ary algorithm integrated with a diffusion-invasion model of glioblastoma,"Physics in medicine and biology, vol. 57, no. 24, p. 8271, 2012.
- [14] R. Rockne, J. Rockhill, M. Mrugala, A. Spence, I. Kalet, K. Hendrickson, A. Lai, T. Cloughesy, E. Alvord Jr, and K. Swanson, "Predicting the efficacy of radiotherapy in individual glioblastoma patients in vivo:a mathematical modeling approach," Physics in medicine and biology, vol. 55, no. 12, p. 3271, 2010.
- [15] R. C. Rockne, A. D. Trister, J. Jacobs, A. J. Hawkins-Daarud, M. L.Neal, K. Hendrickson, M. M. Mrugala, J. K. Rockhill, P. Kinahan, K. A. Krohn et al., "A patient-specific computational model of hypoxiamodulated radiation resistance in glioblastoma using 18f-fmiso-pet," Journal of The Royal Society Interface, vol. 12, no. 103, p. 20141174, 2015.

- [16] 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," Physics in medicine and biology, vol. 59, no. 3, p. 771, 2014.
- [17] J. Unkelbach, B. H. Menze, E. Konukoglu, F. Dittmann, M. Le, N. Ayache, and H. A. Shih, "Radiotherapy planning for glioblastoma based on a tumor growth model: improving target volumedelineation," Physics in medicine and biology, vol. 59, no. 3, p. 747, 2014.
- [18] M. L e, J. Unkelbach, N. Ayache, and H. Delingette, "Gpssi: Gaussian process for sampling segmentations of images," in Medical Image Computing and Computer-Assisted Intervention–MICCAI 2015. Springer, 2015, pp. 38–46.
- [19] B. Menze, A. Jakab, S. Bauer, J. Kalpathy-Cramer, K. Farahani et al., "The multimodal brain tumor image segmentation benchmark (BRATS)," Medical Imaging, IEEE Transactions on, vol. 34, no. 10, pp. 1993– 2024, 2015.
- [20] A. Gooya, K. M. Pohl, M. Bilello, L. Cirillo, G. Biros, E. R. Melhem, and C. Davatzikos, "GLISTR: glioma image segmentation and registration," IEEE TMI, vol. 31, no. 10, pp. 1941–1954, 2012.
- [21] M. Le, H. Delingette, J. Kalpathy-Cramer, E. R. Gerstner, T. Batchelor, J. Unkelbach, and N. Ayache, "Bayesian personalization of brain tumor growth model," in Medical Image Computing and Computer-Assisted Intervention–MICCAI 2015. Springer, 2015, pp. 424–432.
- [22] E. Konukoglu, O. Clatz, P.-Y. Bondiau, H. Delingette, and N. Ayache, "Extrapolating glioma invasion margin in brain magnetic resonance images: Suggesting new irradiation margins," Medical image analysis, vol. 14, no. 2, pp. 111–125, 2010.
- [23] H. Yoshida and M. Nagaoka, "Multiple-Relaxation-Time LBM for the convection and anisotropic diffusion equation," Journal of Computational Physics, vol. 229, no. 20, 2010.
- [24] D. Yu, R. Mei, L.-S. Luo, and W. Shyy, "Viscous flow computations with the method of lattice Boltzmann equation," Progress in Aerospace Sciences, vol. 39, no. 5, pp. 329–367, 2003.
- [25] O. Clatz, M. Sermesant, P.-Y. Bondiau, H. Delingette, S. K. Warfield, G. Malandain, and N. Ayache, "Realistic simulation of the 3-D growth of brain tumors in MR images coupling diffusion with biomechanical deformation," IEEE TMI, vol. 24, no. 10, pp. 1334–1346, 2005.
- [26] K. Swanson, R. Rostomily, and E. Alvord, "A mathematical modeling tool for predicting survival of individual patients following resection of glioblastoma: a proof of principle," British journal of cancer, vol. 98, no. 1, pp. 113–119, 2008.
- [27] A. L. Baldock, K. Yagle, D. E. Born, S. Ahn, A. D. Trister, M. Neal, S. K. Johnston, C. A. Bridge, D. Basanta, J. Scott et al., "Invasion and proliferation kinetics in enhancing gliomas predict idh1 mutation status," Neuro-oncology, vol. 16, no. 6, pp. 779–786, 2014.
- [28] C. E. Rasmussen, "Gaussian processes to speed up hybrid Monte Carlo for expensive Bayesian integrals," vol. 7, 2003, pp. 651–659.
- [29] J. O. Deasy, A. I. Blanco, and V. H. Clark, "Cerr: a computational environment for radiotherapy research," Medical physics, vol. 30, no. 5, pp. 979–985, 2003.

- [30] A. Gooya *et al.*, "GLISTR: Glioma image segmentation and registration," *IEEE Trans. Med. Imag.*, vol. 31, no. 10, pp. 1941–1954, Oct.2012.
- [31] B. H. Menze *et al.*, "A generative approach for image-based modeling of tumor growth," in *Proc. IPMI*, 2011.
- [32] 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.
- [33] B. H. Menze, K. Van Leemput, A. Honkela, E. Konukoglu, M.-A. Weber, N. Ayache, and P. Golland, "A generative approach for image- based modeling of tumor growth," in IPMI. New York: Springer, 2011, pp. 735–747.
- [34] 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.

- [35] 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.
- [36] 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.

[37] 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.
- [38] M. Lê, J. Unkelbach, N. Ayache, and H. Delingette, "GPSSI: Gaussian process for sampling segmentations of images," in MICCAI. New York: Springer, 2015.
- [39] J. Unkelbach et al., "Radiotherapy planning for glioblastoma based on a tumor growth [68] S. Zhang,Y. Zhan, and D. N. Metaxas, "Deformable segmentation via sparse shape representation and dictionary learning," *Med. Image Anal.*, v
- [40] 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.
- `[41] 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. (MICCI,2015)*