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Short Communication

Multimodal Image Driven Pancreatic Tumor Growth Prediction

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Keywords

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Abstract

Personalized tumor growth model is valuable in tumor staging and therapy planning. In this paper, we present a patient specific tumor growth model based on longitudinal multimodal imaging data including dual-phase CT and FDG-PET. The model was evaluated by comparing the predicted tumors with the observed tumors in terms of intracellular volume fraction of tumor surface on six patients with pathologically confirmed pancreatic neuroendocrine tumors, and the results demonstrated the promise of the proposed method.

INTRODUCTION

Quantitatively characterizing the tumor spatial-temporal progression is valuable in staging tumor and designing optimal treatment strategies. Swanson et al. (2000) presented a tumor growth model under the assumption of an infiltrative growth of the tumor cells, while considering differences in cell diffusion in white and gray matter. Clatz et al. (2005) modeled locally anisotropic migration patterns by integrating information from diffusion tensor images (DTI). Hogea et al. (2008) included the mechanical properties of the lesion on surrounding structures to model mass effect. In this paper, we presented a comprehensive tumor growth model using multimodal imaging data. The proposed model was evaluated on pancreatic neuroendocrine tumors. A dedicated protocol was developed to accumulate longitudinal CT and FDG-PET of untreated pancreatic tumors. The only work on the pancreatic tumor modeling that we are aware of is the work presented by (Haeno et al., 2012), in which the authors used a compartment model to divide the cell population into three subpopulations: primary tumor cells, metastasis-enabled cells, and metastasized cells.

MATERIAL AND METHODS

The proposed model is formalized as a coupled partial differential equation (PDE) system (a forward problem). The patient specific parameters (control variables) are estimated by fitting the model prediction to the observed tumor leading to a coupled PDE-constrained optimization problem (an inverse problem). To obtain realistic solution, Tikhonov regularization is introduced to regularize the solution. The optimality system is derived and solved by the Finite Difference Method (FDM).

The proposed tumor growth prediction method includes two parts: parameter estimation and evaluation. We introduce intracellular volume fraction (ICVF) as the biomarker for both model parameter estimation and evaluation. In the parameter estimation part, ICVF calculation takes longitudinal dual-phase CT images as inputs. At each time point, ICVF is measured based on pre- and post-contrast CT images. The measured ICVF at the 1st follow-up is compared with the predicted ICVF growing from the base line to find the optimal parameters by minimizing the deviation between the two ICVF maps. Once the model parameter is estimated, the tumor grows from the 1st follow-up with estimated model parameter. The predicted ICVF and the extracted tumor surface are compared with the measured ICVF and tumor surface at the 2nd follow-up for evaluation.

RESULTS

To study tumor growth, we have developed a dedicated protocol spanning for several years to collect patients with pancreatic neuroendocrine tumors. The desirable longitudinal data needs to satisfy the requirements: 1) the tumor should be big enough (volume > 20mm^3) to allow us to ignore the error induced by segmentation and registration, 2) at least three time points and each time point includes both dual-phase CT and FDG-PET, and 3) without any treatments. Usually, a tumor will be surgically removed when it becomes sufficiently big. The contradictive requirements 1) and 3) lead to the difficulty to obtain desirable data (Figure 1).

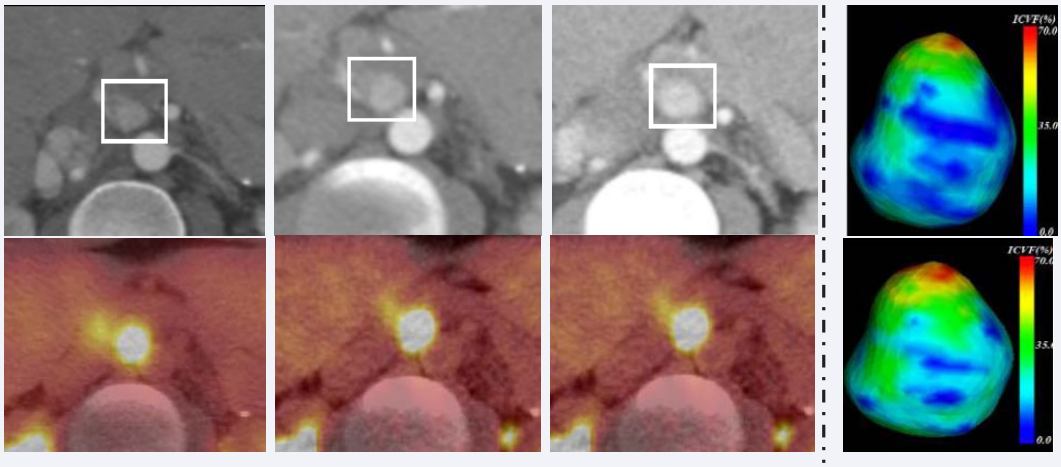

Figure 1 Longitudinal data and prediction results. Left: longitudinal images. The top row is the post-contrast CT and the bottom row is the FDG-PET. From left to right: baseline, the 1st follow up, the 2nd follow up. Right: the top image is the reference ICVF map and the bottom is the predicted ICVF map.

We evaluated the proposed model by comparing the predicted ICFV map with the measured ICVF map at the 2nd follow-up. The predicted ICVF map was produced by growing the ICVF from the 1st follow-up for the period between the 1st and 2nd follow-up with the parameters estimated from the longitudinal data at the baseline and the 1st follow-up. The predicted tumor is an isosurface extracted from the predicted ICVF map based on a threshold. The left side of Figure 1 shows the longitudinal post-contrast CT and FDG-PET. The right side of Figure 1 shows the reference ICVF map and the predicted ICVF map. The predicted ICVF map has quite similar ICVF distribution as the reference ICVF map by visual inspection. Quantitatively, the average ICVF difference between them is 2.6 $\pm$ 0.8% for six patients.

CONCLUSIONS AND FUTURE WORK

In this paper, we presented a tumor growth model, which is characterized by being driven by routine clinical imaging data based on ICVF. The experiment on pancreatic neuroendocrine tumors demonstrated the promise of the proposed model. Other than the characteristics of tumor itself such as the aggressiveness measured by the metabolic rate, tumor microenvironment is also essential for the study of tumor growth. In the future, besides dual-phase CT and FDG-PET, we will introduce DCE-MRI to measure vasculature/perfusion regions and FMISO-PET to measure hypoxia regions in order to model tumor microenvironment.

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