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A mass transfer model for computational prediction of proliferation and therapy outcome of non-Hodgkin lymphoma

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ABSTRACT

Mathematical modeling constitutes an emerging area of oncological research aiming to predict spatial and temporal evolution of tumors, by describing many different phenomena, which occur at different scales. Among these, modeling at the macroscopic scale has an interesting potential of application, when applied in a framework where actual diagnostic imaging is used to identify the metabolic tumor volume undergoing proliferation.

Diffuse large B-cell lymphoma (DLBCL) is a cancer of B cells, a type of lymphocyte that is responsible for producing antibodies. The most common form of Non-Hodgkin lymphoma among adults, DLBCL can arise in any part of the body and may play a very aggressive malignancy. This paper aims to enforce a mass transfer modeling approach in order to gain deeper insight into the dynamics of tumor growth at the tissue scale and to develop a predictive, quantitative method for each patient at hand. A cohort of 18 patients has been successfully enrolled to validate the model. Results confirm that tumor proliferation, at the macroscopic scale, scores many nonlinear features, and show that the proposed model could be used by oncologists as a decision support tool towards personalized treatment optimization of solid tumors.

1. Introduction

Diffuse large B-cell lymphoma (DLBCL) accounts for 30–35% of non-Hodgkin lymphoma cases [1]. Patient survival is extremely variable since DLBCL constitutes a heterogeneous disease. A high degree of prognosis evaluation is performed via some international prognostic indices (IPI), for those patients who are at risk of early relapse/progression [2]. Nevertheless, efforts are being made to overcome IPI system inconsistency for evaluating patients with intermediate IPI scores [3]. This scenario requires novel biomarkers in DLBCL and how these can be incorporated into current risk-adjustment models for prognosis, but confusion still exists concerning the optimal predictor, which translates the need for further prognostic models, diagnostic tools, and/or their combination.

Over the past decade, Positron emission tomography/computed tomography scan (PET/CT) following injection of ^{18}F fluorodeoxyglucose (FDG) has been widely used for patient evaluation in lymphoma [4–7]. Recent studies have found that metabolic tumor volume (*MTV*) represents a reliable prognostic marker in solid tumors [8,9] as well as in lymphomas. ^{18}F FDG PET/CT imaging offers functional tissue characterization to accurately reflect the metabolic activity of a lesion that can occur in a spontaneous neoplasm e.g. in the case of progression or following therapy in the hypothesis of a remission. These variations can therefore be monitored over time and evidently reproduced on mathematical models.

From a materials science perspective, cancer is a multiscaled substrate, bearing nonlinear couplings between the nanoscale (genomics), the microscale (cell signals/molecular biology) and the macroscale (tumor mass dynamics). This variety of scales has been attacked so far in a vast body of literature [10–12], the most promising so far being the project by Stamatakos and co-workers [13]. Among the proposed cancer mass transfer, the continuum mechanics approach exploiting a set of

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