ABSTRACT

Recent advances in image-guided and adaptive radiotherapy have ushered new requirements for using single and/or multiple-imaging modalities in staging, treatment planning, and predicting response of different cancer types. Quantitative information analysis from multi-imaging modalities, known as ‘radiomics’, have generated great promises to unravel hidden knowledge embedded in imaging for mining it and its association with observed clinical endpoints and/or underlying biological processes. In this chapter, we will review recent advances and discuss current challenges for using radiomics in radiotherapy. We will discuss issues related to image acquisition, registration, contouring, feature extraction and fusion, statistical modeling, and combination with other imaging modalities and other ‘omics’ for developing robust models of treatment outcomes. We will provide examples based on our experience and others for predicting cancer outcomes in radiotherapy generally and brain cancer specifically, and their application in personalizing treatment planning and clinical decision-making.
INTRODUCTION

kV x-ray computed tomography (kV-CT) has been historically considered the standard modality for treatment planning in 3D conformal (3DCRT) or intensity-modulated radiotherapy (IMRT) because of its ability to provide electron density information for heterogeneous dose calculations (Khan & Gerbi, 2012; Webb, 2001). However, additional information from other imaging modalities could be also used to improve treatment monitoring and prognosis in different cancer sites (El Naqa et al., 2009; Kumar et al., 2012; Lambin et al., 2012). Physiological information (tumor metabolism, proliferation, necrosis, hypoxic regions, etc.) can be collected directly from nuclear imaging modalities such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) or indirectly from magnetic resonance imaging (MRI) (Condeelis & Weissleder, 2010; Willmann, Van Bruggen, Dinkelborg, & Gambhir, 2008). For instance, changes in tumor volume captured on CT images may be predictive of local control in lung cancer (Ramsey et al., 2006; Seibert et al., 2007). In addition, functional/molecular imaging and in particular 2-deoxy-2-[18F]fluoro-D-glucose (FDG) PET, a glucose metabolism analog, has shown promise as a potential prognostic factor for predicting radiotherapy efficacy or potential side effects. The primary focus in the literature to this point has been directed towards simple metrics describing $^{18}$F-FDG PET images, especially maximum standardized uptake values ($\text{SUV}_\text{max}$). On the other hand, dynamic contrast enhanced MRI (DCE-MRI), a perfusion surrogate, was tested in the rat brain to monitor radiation-induced adverse effects on healthy tissues (Constanzo et al., 2016) or assessing tumor physiological characteristics (Hormuth, Skinner, Does, & Yankeelov, 2014; Poulin et al., 2015), and used to assess treatment response of soft tissue sarcoma (Shapeero, Vanel, Verstraete, & Bloem, 2002; van Rijswijk et al., 2003; Vanel et al., 2004). Also, apparent diffusion coefficients (ADC) values from diffusion-weighted MRI (DW-MRI), a measure of water molecules diffusion (Brownian motion) in tissue, were significantly correlated with sarcoma response to radiotherapy (Einarsdóttir, Karlsson, Wejde, & Bauer, 2004). However, only sparse reports focused on radiation-induced grey matter damage, as for example Horská et al., who studied subcortical changes after cranial radiation therapy in children (Horská et al., 2014).

Advances in delivery and imaging technologies put a step forward into a new era of image-guided and adaptive radiotherapy (IGART), which has witnessed burgeoning interest in applying different imaging modalities, both to define the target volume and to predict treatment response. In modern IGART, there is a strong interest for using multimodal imaging in tumor staging and optimizing the treatment planning of different cancer types (Jaffray, 2012). The goal is to achieve improved target definition by incorporating complementary anatomical information
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