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Physics Contribution

Comprehensive Population-Averaged Arterial Input Function for Dynamic Contrast–Enhanced vMagnetic Resonance Imaging of Head and Neck Cancer

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Summary

The use of population-averaged arterial input functions (PA-AIFs) makes DCE-MRI studies more time- and cost-efficient. This study generates a PA-AIF specific to the head and neck region, based on data from the right and left carotid arteries and from 3 different time points. This AIF is valid for both left- and right-sided malignancies both before and during treatment, though a time-point-specific AIF may improve pharmacokinetic parameter accuracy.

Purpose: To generate a population-averaged arterial input function (PA-AIF) for quantitative analysis of dynamic contrast-enhanced MRI data in head and neck cancer patients.

Methods and Materials: Twenty patients underwent dynamic contrast-enhanced MRI during concurrent chemoradiation therapy. Imaging consisted of 2 baseline scans 1 week apart (B1/B2) and 1 scan after 1 week of chemoradiation therapy (Wk1). Regions of interest (ROIs) in the right and left carotid arteries were drawn on coronal images. Plasma concentration curves of all ROIs were averaged and fit to a biexponential decay function to obtain the final PA-AIF (AvgAll). Right-sided and left-sided ROI plasma concentration curves were averaged separately to obtain side-specific AIFs (AvgRight/AvgLeft). Regions of interest were divided by time point to obtain time-point-specific AIFs (AvgB1/AvgB2/AvgWk1). The vascular transfer constant (K_{trans}) and the fractional extravascular, extracellular space volume (V_e) for primaries and nodes were calculated using the AvgAll AIF, the appropriate side-specific AIF, and the appropriate time-point-specific AIF. Median K_{trans} and V_e values derived from AvgAll were compared with those obtained from the side-specific and time-point-specific AIFs. The effect of using individual AIFs was also investigated.

Results: The plasma parameters for AvgAll were $a_{1,2} = 27.11/17.65$ kg/L, $m_{1,2} = 11.75/0.21$ min^{-1}. The coefficients of repeatability (CRs) for AvgAll versus AvgLeft were 0.04 min^{-1} for K_{trans} and 0.02 for V_e. For AvgAll versus AvgRight, the CRs were 0.08 min^{-1} for K_{trans} and 0.02 for V_e. When AvgAll was compared with AvgB1/AvgB2/AvgWk1, the CRs were slightly higher: 0.32/0.19/0.78 min^{-1}, respectively, for K_{trans}; and 0.07/0.08/0.09 for V_e. Use of a PA-AIF was not significantly different from use of individual AIFs.

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Conflicts of interest: none.

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Conclusion: A PA-AIF for head and neck cancer was generated that accounts for differences in right carotid artery versus left carotid artery, day-to-day fluctuations, and early treatment-induced changes. The small CRs obtained for K_{trans} and V_e indicate that side-specific AIFs are not necessary. However, a time-point-specific AIF may improve pharmacokinetic accuracy. © 2014 Elsevier Inc.

Introduction

Approximately 50,000 people in the United States are diagnosed annually with head and neck cancer (HNC) (1). The TNM (tumor, nodes, metastasis) staging system constitutes the primary means of determining disease prognosis. However, identically staged cancers will often respond differently to the same treatment, and the TNM system is insensitive to this issue. Recent investigations have identified several functional imaging modalities that may improve the ability to evaluate disease response/progression and more accurately predict clinical outcome (2-6). Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is one such method.

Dynamic contrast-enhanced MRI is a noninvasive imaging technique that monitors the passage of a contrast agent bolus through a patient's vasculature. As it travels, the contrast agent diffuses into interstitial space and out again in a matter of seconds. This diffusion happens to a small extent in all tissues, but it happens to a greater extent in tumors, which are often characterized by leaky microvasculature (7). Signal enhancement is thus greater in tumors than in normal tissues. Analysis of the magnitude and rate of this signal enhancement yields valuable information about tumor perfusion, vascular density, and vascular permeability (collectively termed "pharmacokinetic parameters") that can be used to evaluate disease progression, define tumor boundaries, and assess response to therapy (8-12).

One of the commonly used techniques for determining contrast agent kinetics was described by Tofts et al (13). Briefly, this 2-compartment model characterizes the exchange of contrast agent between the vasculature and the extravascular extracellular space. The rate constant for this process is K_{trans}, which is related both to the amount of blood flow through the tissue and to the permeability of the vasculature.

The validity of any DCE-MRI study rests on its ability to obtain accurate pharmacokinetic (PK) parameters, which in turn requires an accurate arterial input function (AIF) (14). The AIF is the time course of the contrast agent concentration in the arterial blood. Ideally, an individual AIF should be calculated for each patient at each imaging session. Clinically, however, this process is too costly and time-consuming to be practical. Furthermore, the imaging field of view may not contain an artery from which to measure an AIF (15). The use of a population-averaged AIF (PA-AIF) would help simplify and shorten DCE-MRI protocols, provided it did not significantly affect PK parameter values. Studies in the abdomen (15), breast (16), prostate (17), osteosarcomas (18), and neck lymph node metastases (11) have shown that PK parameters based on a PA-AIF are not statistically different from PK parameters obtained using individual AIFs.

The goal of this study was to calculate a PA-AIF specific to the head and neck region based on data from the right and left carotid arteries (RCA and LCA), 2 pretreatment scans, and 1 scan after 1 week of treatment. Such an AIF would enable future head and neck DCE-MRI studies to be more cost and time efficient.

Methods and Materials

Clinical protocol

Written informed consent was obtained from 20 patients who were enrolled in an institutional review board–approved clinical trial in the Department of Radiation Oncology at the Duke Cancer Institute. All patients had locally advanced squamous cell HNC and were undergoing curative intent concurrent chemoradiation (CRT). Details of this treatment have been published elsewhere (19). Each patient received 3 DCE-MRI scans at 3 different time points: 2 pretreatment baseline scans approximately 1 week apart (B1 and B2) and 1 scan that occurred after completion of the first week of CRT (Wk1). Each patient also underwent diffusion-weighted MRI scans and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET)/computed tomography scans at the same 3 time points. Findings involving diffusion-weighted MRI are pending, whereas findings from the FDG-PET study have already been reported by Hoang et al (19).

MRI protocol

The MR images were acquired on a 1.5-T scanner (SignaExcite; GE Medical Systems, Waukesha, WI, software versions 14x and 15x) in the Department of Radiation Oncology. After a single bolus injection of 0.1 mmol/kg gadopentetic acid (Gd-DTPA/Magnevist; Berlex Laboratories, Wayne, NJ), the entire head and neck region was imaged using a dynamic coronal 3-dimensional fast gradient echo sequence: time to repetition, 5.8-6.6 ms; time to echo, 1.8-2.0 ms; field of view, 24 × 24 cm^2; matrix size, 256 × 256; temporal resolution, 10 s; number of scans, 19-32; slice thickness, 10 mm; and flip angle, 60° (7). Imaging