Perfusion and Permeability Imaging for Head and Neck Cancer

Theory, Acquisition, Postprocessing, and Relevance to Clinical Imaging

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KEYWORDS

• Head and neck cancer • Perfusion • Permeability • MR imaging • CT

KEY POINTS

- Perfusion imaging is the study of tissue circulation at the capillary level.
- Perfusion and permeability imaging are closely related but assess different characteristics of the movement of contrast tracers from the intravascular plasma to the tissue interstitial space and back again.
- The analysis of perfusion and permeability clinical imaging data relies on algorithms designed to model the underlying physiologic processes. The analysis of the acquired imaging data depends greatly on the assumptions of the model chosen.
- The acquisition protocols should be carefully designed and matched to the type of perfusion and/or permeability imaging performed and must obtain the data necessary to satisfy the requirements of the model chosen.
- Perfusion and permeability imaging provide powerful clinical information affecting the diagnosis, prognosis, and treatment of head and neck cancer.

INTRODUCTION

Radiologists are exposed to 2 different paradigms within the practice of perfusion imaging. First, they are occupied with perfusion imaging for central nervous system (CNS) pathologic conditions, most commonly ischemic stroke and tumors. These pathologic conditions occur within a system protected by a blood-brain barrier (BBB) that dictates the type of perfusion models that can be applied. The BBB represents the impermeability of the vessel wall to large molecules, including contrast agents. These pathologic conditions disrupt the normal physiologic mechanisms and structural barriers that create the BBB and result in both a characteristic radiographic appearance and a perfusion dynamic that generates diagnostic information. Conversely, the head and neck soft tissue structures, like the rest of the body, are governed by a different set of physiologic mechanisms and, consequently, a different perfusion model, typically referred to as permeability, which is

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defined by the passage of these same large molecules across the capillary wall and into the interstitial space (IS). It has been demonstrated that studying the perfusion characteristics of head and neck tumors improves historadiologic diagnosis, correlates with response to treatment, and predicts the potential for recurrence. How clinicians acquire radiographic images and model these physiologic processes, and how data are analyzed, profoundly alters the resultant data and the interpretation of the study. Consequently, diagnostic and prognostic opinion depends on the initial acquisition and postprocessing choices. This article focuses on the theoretic and technical processes that are fundamental to perfusion, and particularly on permeability imaging, using an explanatory method without the use of complicated mathematics.

PERFUSION FUNDAMENTALS

Perfusion Imaging Basics

In essence, perfusion imaging is the study of the microcirculation at the capillary level. There is, unfortunately, confusion created by the nomenclature. Perfusion is often used as a unifying term to describe the entire medical discipline of the study of dynamic contrast-enhanced (DCE) imaging. When it is applied to simple systems in which only the vasculature can be measured (eg, the brain), it is termed perfusion. When applied to the remainder of the body, where there is passage of contrast into the extracellular extravascular space (EES) also known as the Interstitial Space (IS), it is termed permeability. Care must be taken not to confuse the general term perfusion with the more specific term perfusion or its counterpart permeability.

In medicine, a tracer (or indicator) is defined as a detectable substance introduced into a dynamic biological system that acts in a physiologic manner to provide information about the function of the system. Within clinical imaging there is a myriad selection of tracers, including iodinated contrast agents, gadolinium-based contrast agents, nuclear isotope tagged molecules, and the like. The total amount of the indicator within a given volume of tissue is termed the concentration of the indicator. For imaging purposes, it is typically normalized to a given volume of tissue in milliliters, using the nomenclature concentration of tissue (Ct). This should not be confused with the concentration of an indicator at a given amount of time (C[t]).

Within the brain parenchyma, the impermeable BBB creates a simplified system because contrast material remains within the vascular network and does not pass into the EES. The vascular space may be divided into the cellular component, which is most pragmatically represented by hematocrit (Hct) and the plasma, in which the contrast material is contained. The extravascular space may be considered the IS and the intracellular space. Brain models of perfusion are typically perfusion only; there is no passage of contrast to the IS to complicate the analysis.

For the measurement of contrast within the vascular space, or if the BBB is disrupted, the EES is represented either by signal intensity change (for MR imaging) or Hounsfield unit (HU) attenuation change (for computed tomography [CT]). The measurement produces a time concentration curve that represents the tissue blood flow (BFt), tissue blood volume (BVt), and mean transit time (MTT). BFt is the total amount of blood delivered to a given amount of tissue and is expressed in milliliters of blood per minute per 100 mL of tissue. In some models it is simply expressed as flow (F) of blood to the tissue or blood flow (BF). BVt is the total intravascular volume of blood within a given amount of tissue and is expressed in mL/100 mL of tissue. BVt is sometimes abbreviated BV.

Depending on the mode of acquisition and the model being used, the necessary data to quantify perfusion require the contrast concentration of the arterial input to the tissues (arterial input function [AIF]), the concentration of the contrast in the tissues themselves (Ct) and the venous outflow concentration (venous outflow function [VOF]). This last measurement is typically used not for BF purposes but to provide a standard of voxel contrast concentration for normalization of the AIF, which reduces artifact from volume averaging if a small artery is chosen for the AIF that fails to fill the entire voxel adequately.

The concentration curve of contrast in the arteries has a characteristic morphology (**Fig. 1**). It consists of the baseline before vessel opacification, a rapid increase in concentration terminating in a peak, and an initially rapid and then more gradual decline in the magnetic resonance (MR) signal intensity or CT HU attenuation as the contrast leaves the voxel and is cleared systemically by the body. A second small peak in the arterial concentration curve (the AIF) is caused by blood that has passed through the circulatory system and is now reentering the arterial inflow, although it is markedly diluted by the rest of the body BV (recirculation).

The measurement of the Ct of contrast produces a different appearance than the AIF due to dispersion of contrast through the much larger BV of the capillary network, as well as the decreased perfusion pressure with slower velocity. This physiologic phenomenon is critical because it allows for micromolecular passage