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Behind the Technology: CT Perfusion in the Setting of Acute Stroke Management

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Abstract

Computed Tomography Perfusion (CTP) is an imaging modality that generates parametric maps of cerebral hemodynamics which are useful in the assessment of suspected acute ischemic stroke. However, the technology underlying CTP is complex and serious controversy surrounds the safety of CTP tests and the reproducibility and validity of CTP results. This report briefly outlines the history of CTP, its current clinical applications for stroke management, the main controversies surrounding CTP, and future directions for this technology.

Introduction

In the setting of acute stroke, knowledge of the ischemic insult and potential for tissue salvage is critical in clinical decision-making. Dynamic, first-pass computed tomography perfusion (CTP) is an imaging modality that describes the hemodynamics of cerebral tissues.¹ It does so by gathering information about the flow of contrast media through the cerebral vasculature and by calculating perfusion values that describe the blood flow through cerebral tissue beds. CTP is rapidly performed,² commonly accessible,³ and when used alongside other imaging modalities such as non-contrast computed tomography (CT) and CT angiography, improves clinicians' diagnostic abilities in the setting of acute cerebrovascular attack.⁴

But several reports have demonstrated problems with CTP safety,⁵ reproducibility,⁶ and accuracy,⁷ which restrict the unique potential of CTP to produce quantitative perfusion results that are safely obtained and clinically meaningful. One factor that has limited the development of solutions to these problems may be the general confusion surrounding the technology, clinical applications, and controversies in CTP imaging. The purpose of this review was to briefly describe the history, current applications, controversies, and future directions of CTP in the context of acute stroke management.

History of CTP

In 1897 Stewart⁸ introduced the indicator-dilution theory for measurement of cardiac output and in 1954 Meier and Zierler⁹ built upon this work by presenting their theory of the indicator-dilution method for measurement of blood flow and volume, which states the basic relationship that, for a normal physiologic tissue bed, blood volume equals blood flow times the mean circulation time ($V = F \times MT$). In 1980 Axel¹⁰ first conceptualized the use of Computed Tomography (CT) in conjunction with a non-diffusible tracer to measure cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT). Axel suggested that the central volume principles set forth by Meier and Zierler could be applied to CT-acquired data to successfully generate information about the blood flow in cerebral tissues.

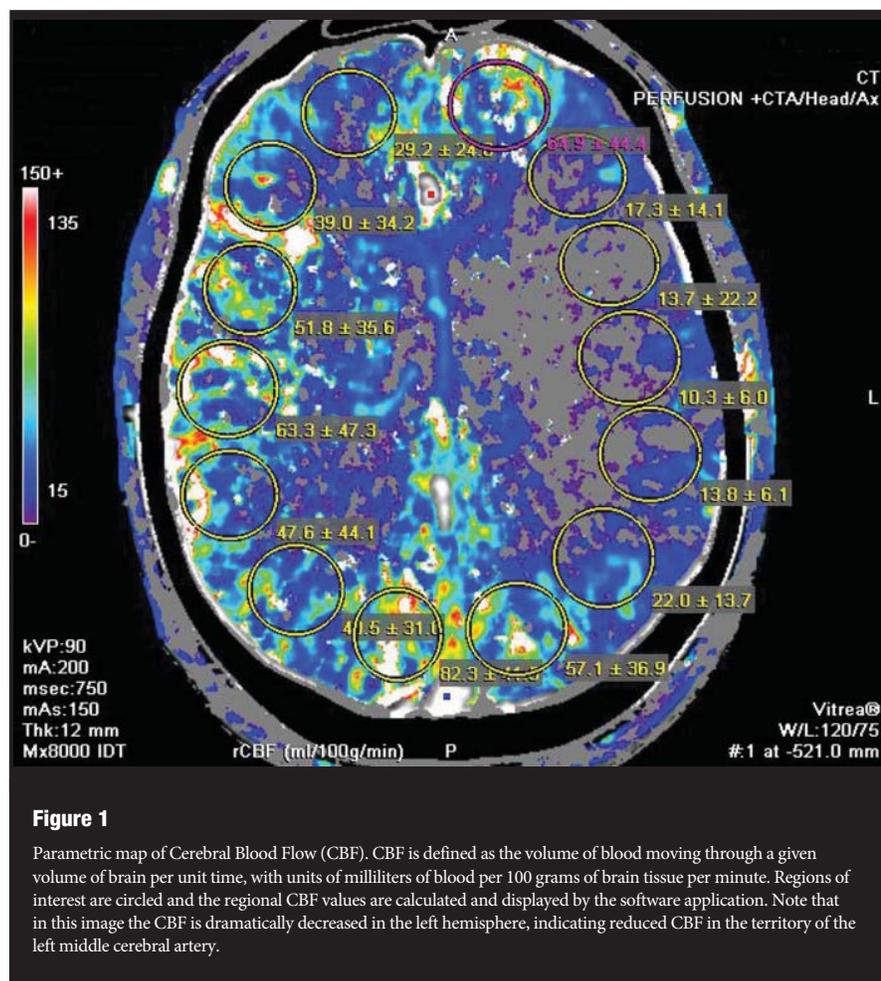


Figure 1

Parametric map of Cerebral Blood Flow (CBF). CBF is defined as the volume of blood moving through a given volume of brain per unit time, with units of milliliters of blood per 100 grams of brain tissue per minute. Regions of interest are circled and the regional CBF values are calculated and displayed by the software application. Note that in this image the CBF is dramatically decreased in the left hemisphere, indicating reduced CBF in the territory of the left middle cerebral artery.

The recent development of high-speed helical or spiral CT scanners provided the machinery for CTP theory to be translated into practice.³ Furthermore, the development of computer software applications that process CT source images and generate perfusion maps enabled stroke management teams to simply and rapidly acquire cerebral perfusion data.¹¹ Today, high-speed CT scanners are commonplace in U.S. hospitals and the entire CTP imaging process can be performed in a matter of minutes.²

Current applications

At our institution, patients who present with acute stroke symptoms are managed with a multi-pronged diagnostic algorithm. The first diagnostic test is always a non-contrast CT scan of the brain, which is used to rule-out cerebral hemorrhage, hematoma, and other lesions. Secondary tests include CT angiography and CTP. CT angiography examines the neck and head vasculature for vessel occlusion or rupture. This information is used to locate the pathology and determine whether endovascular treatments, such as thrombectomy, are warranted. CTP examines ischemic cerebral tissues and differentiates between irreversibly infarcted tissue, called the infarct core, and potentially salvageable tissue, called the penumbra.

It has been argued that infarct core has three characteristic features: (1) an elevated MTT (it takes more time for blood to traverse the ischemic tissue); (2) a reduced CBF (the velocity of blood flow through ischemic tissue is decreased); and (3) a reduced CBV (the volume of blood in the ischemic tissue is decreased).³ In

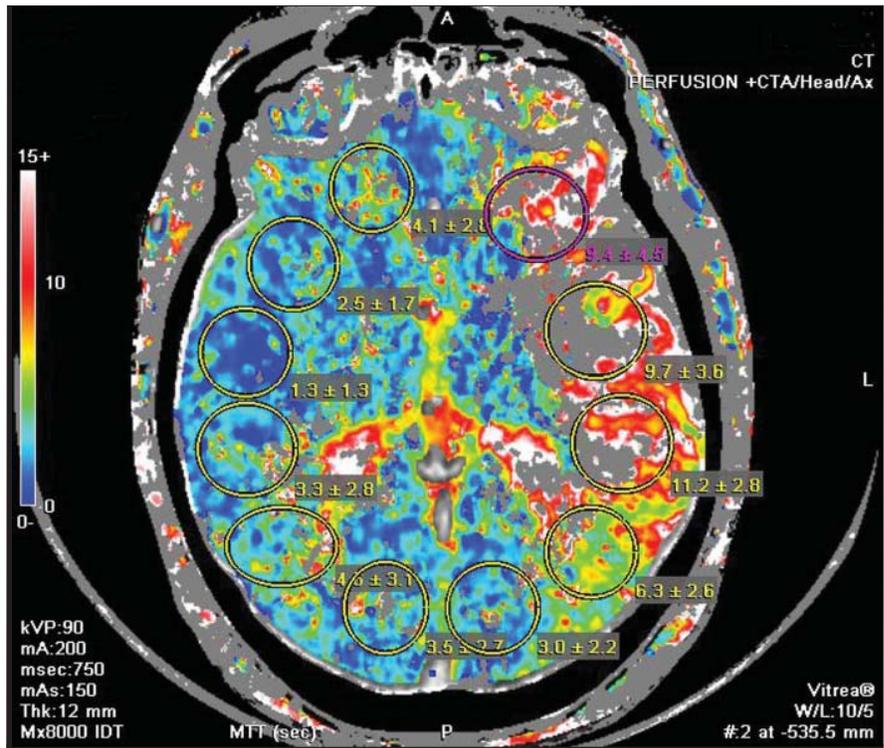


Figure 2

Parametric map of Mean Transit Time (MTT). MTT is defined as the average transit time of blood through a given brain region, measured in seconds. In this image the MTT is increased in the left hemisphere relative to the right, indicating a reduced velocity of blood flow in the territory of the left middle cerebral artery.

comparison, penumbra also demonstrates an elevated MTT and a reduced CBF. However, in penumbra the CBV is not reduced; it remains level or may even be elevated, due to collateral

circulation via uninjured arterial and leptomeningeal territories.² Thus, assuming that MTT is elevated and CBF is reduced, a mismatch in CBV may determine candidacy for

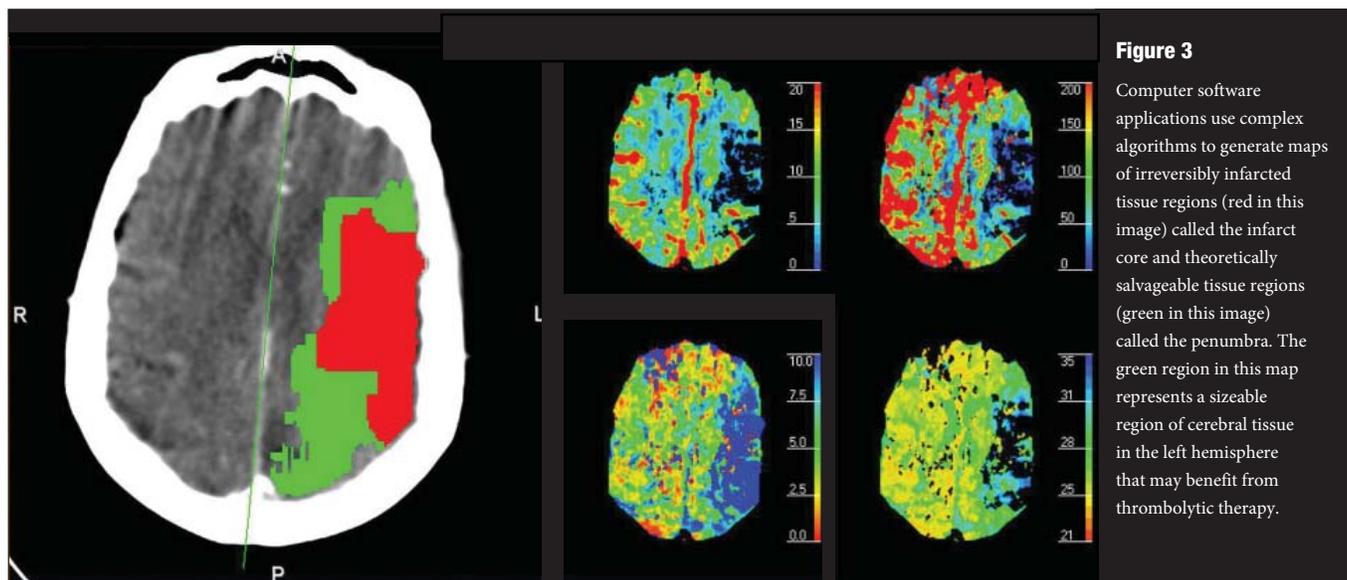


Figure 3

Computer software applications use complex algorithms to generate maps of irreversibly infarcted tissue regions (red in this image) called the infarct core and theoretically salvageable tissue regions (green in this image) called the penumbra. The green region in this map represents a sizeable region of cerebral tissue in the left hemisphere that may benefit from thrombolytic therapy.

thrombolytic therapy, with a level or elevated CBV indicating treatment and a reduced CBV contraindicating treatment.³

Penumbra may be salvaged if blood flow restoration is rapidly achieved. Therapeutic agents, such as thrombolytics, aid clot dissolution and are considered when there is extensive penumbra.² Yet the decision to use thrombolytic agents is not without risk as these medications may also induce severe hemorrhage. Therefore, the potential benefits of the recanalization of arteries supplying injured but salvageable tissue must be weighed against the potential morbidity and mortality associated with hemorrhage.³

Stroke management is a complex, team-oriented process. Image source data gathered in the Emergency Department by the CT scanner is transmitted over the computer network to neuroradiologists who process the data using commercial software applications to generate CTP parametric maps. These images are interpreted by neuroradiologists and are also passed to neurosurgeons. Dialogue between neuroradiologists, neurosurgeons, and neurologists consider all three studies—non-contrast CT, CT angiography, and CTP—to arrive at treatment decisions. Of course, effective communication between members of the stroke team and efficiency are paramount in the setting of acute stroke; as the saying goes, “time is brain.”

Controversies

Several controversies surround CTP, including the risk of radiation exposure to patients. For instance, a July 2010 *New York Times* report⁵ highlighted the stories of scores of patients that have recently been exposed to radiation overdoses during CTP scans in hospitals across the U.S. On the other hand, the CTP radiation doses reported in the medical literature have generally been safe; as one review article stated, the radiation exposure in a typical CTP scan is approximately equal to the background radiation a person living in Boston, Massachusetts is exposed to in a given year.¹ The radiation controversy partially hinges on the balance of radiation dose with image quality, and several authors¹²⁻¹⁴ have explored methods to achieve adequate image resolution and signal-to-noise while limiting radiation doses by altering the image acquisition frequency settings of CT scanners. This controversy also centers on the degree of automation that CT scanners use to calculate radiation doses; some experts argue

that automation will lead to more appropriate dosing while others argue that unchecked automation may lead to unnecessary overdosing.⁵

Another controversy surrounding CTP is the variability of quantitative results. Studies have shown that multiple factors affect the perfusion maps that are generated by software applications. For example, software operator differences have led to significantly different perfusion results.^{6,15} More recently, differences between software applications have been shown to generate significantly different results as well.⁷ Put differently, it is possible that identical source imaging data for a given patient will yield significantly different CTP results if processed by different operators or by different software applications. For these reasons, quantitative perfusion results have been traditionally interpreted with caution. Yet there is motive for improved reproducibility and accuracy of CTP results, because these values could be used to develop definitive perfusion thresholds for use in clinical decision-making, particularly the use of thrombolytic therapy, such as tissue plasminogen activator (tPA).¹⁶

Future directions

The stroke imaging community has identified two important steps for the improvement of CTP; standardization of CTP scanning and standardization of CTP post-processing.¹⁷ Progress is being made in both these aims. For instance, in September, 2007, consensus-based imaging acquisition protocols (including suggested radiation doses) for CTP were drafted at an international symposium of experts in the field.¹⁷ Additionally, efforts to improve the accuracy and reliability of CTP through the development of a digital phantom data set against which commercial software platforms can be evaluated are currently underway.¹⁸

Conclusion

CTP is a rapidly developing diagnostic imaging tool that is useful in acute stroke diagnosis. Standardization of this technology may enable clinical decision-making based on quantitative data.

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