**CT Perfusion Imaging of the Brain**

- CT perfusion (CTP) imaging displays information about capillary-level hemodynamics in the brain parenchyma that may be of value in acute stroke patients for determining the extent of both the (1) irreversibly infarcted ("core") and (2) severely ischemic but potentially salvageable, "at-risk" tissue ("penumbra")

- CTP is used to estimate infarct core in acute stroke patients for whom MR-DWI (diffusion weighted imaging) cannot be obtained in a timely manner or is contra-indicated, typically after a non-contrast CT (NCCT) has excluded hemorrhage, and CT angiography (CTA) has demonstrated an intravascular occlusion that can be a target for endovascular therapy

- CTP may also be used to diagnose and classify brain ischemia associated with transient ischemic attacks or vasospasm following aneurysmal subarachnoid hemorrhage

- Strict protocol rules at Mass General Imaging ensure that the radiation dose for CTP is as low as reasonably achievable. The total radiation exposure is substantially less than the FDA recommended maximum dose of 500 mGy

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**CT and MR perfusion imaging of acute stroke patients can help to distinguish irreversibly infarcted brain tissue, the stroke core, from severely ischemic but potentially salvageable tissue, the "at-risk" penumbra. "Mismatch" occurs when the volume of penumbra is substantially larger than that of the core. The degree of mismatch may help guide management decisions, including determining whether a patient may benefit from reperfusion therapies beyond the 4.5-hour window for intravenous thrombolysis supported by the ECASS 3 and SITS-ISTR studies. Moreover, there is increasing evidence that the core/penumbra mismatch may persist for 12 or even 24 hours after the onset ischemia, and hence, the potential role of advanced imaging for patient selection for endovascular treatments beyond 6 to 9 hours is currently under intense study. Other proposed indications for CTP imaging include (1) increasing the sensitivity and specificity of stroke diagnosis over that of NCCT and CTA when MR-DWI cannot be obtained in a timely manner or is contra-indicated, (2) determining stroke etiology and stroke subtype, and (3) helping to guide additional management decisions, such as those involving hypertensive treatment, the degree and frequency of monitoring, and disposition (based on the possibility of delayed worsening).

The imaging algorithm for evaluation of a patient who arrives at Mass General with symptoms of acute stroke or transient ischemic attack (TIA) begins with a non-contrast CT (NCCT) to establish whether there is a hemorrhage, an absolute contraindication to IV thrombolysis (Figure 1). NCCT is followed by CT angiography (CTA), to determine whether there is an intravascular occlusion that may be a target for endovascular treatment (intra-arterial thrombolysis or clot retrieval devices) up to 9 hours post stroke onset. Because DWI is the most accurate means of determining infarct core, MRI is the next preferred imaging modality if it can be rapidly obtained. An infarct core larger than one-third of the middle cerebral artery territory, approximately 100 ml, is considered to be a contraindication to reperfusion therapy. MR perfusion imaging (MRP) is typically obtained following DWI, unless its acquisition would delay intra-arterial therapy or is otherwise not appropriate.

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**Figure 1.** Imaging algorithm for acute stroke recommended by Mass General neuroradiology.
MRI, however, is not suitable for some patients due to contraindications such as pacemakers, aneurysm clips, or other devices, or because they are unable to cooperate and remain still during the MRI exam. In these patients, CTP can be used to evaluate the extent and degree of ischemic brain parenchyma. Although there is no perfusion measure that is as reliable as DWI for identification of infarct core, current thinking is that regions of markedly diminished cerebral blood flow (70-80% reduction in CBF) provide the most accurate possible CT estimate of DWI-defined infarct core. Regions of reduced cerebral blood volume (CBV) are more variable both physiologically and with regard to technical parameters. Potentially salvageable "at-risk" regions of ischemic penumbra, the target for reperfusion therapy, typically show more modest reductions of blood flow, with concomitant increase in mean transit time (MTT delayed > 150%). A mild, less than 50%, decrease in CBF most often reflects "benign oligemia" rather than true ischemic penumbra, and may indeed be associated with elevated CBV (hyperemia secondary to autoregulatory vasodilatation), a phenomenon that has been previously described on PET studies.

### CTP Examination

Currently, the standard protocol for CTP neuroradiology examinations performed at MGH uses the "shuttle mode" feature of our volume CT scanners, covering a total of ≥8 cm through the brain. This is sufficient for evaluation of all anterior circulation strokes with a single acquisition using a single 35 ml bolus of IV contrast, with one image collected every 3 seconds for approximately 90 seconds, and X-ray energy level settings of 80 kVp and 150 mAs per rotation. Post-processing algorithms, based on mathematical modeling of the changes in signal intensity over time accompanying the intravenous administration of contrast, are used to estimate the cerebral blood volume (CBV), blood flow (CBF), and mean transit time (MTT) within each voxel of tissue. CBV, CBF, and MTT color-coded maps can be generated (Figure 2) to show the variations in these measures.

Because of the long duration of repetitive ("cine") imaging over a single brain region associated with CTP scanning, there is a risk of excessive radiation exposure if the X-ray energy settings for CTP image acquisition are inappropriately high; a risk not typically present with routine unenhanced brain CT and CTA. In the fall of 2009, the FDA issued a notification regarding an investigation of a single facility where a number of patients received excessive radiation exposure from CTP exams up to eight times the maximum FDA recommended dose. Subsequently, this problem was also discovered at a small number of other stroke centers, where the standard scan parameters for CTP acquisition, as suggested in the literature and accepted by the stroke imaging community for over a decade, were similarly not followed. A substantial proportion of those patients experienced transient hair loss a few weeks after admission, an effect that has been associated with cumulative exposure to 3-5 Gray (Gy) absorbed dose of ionizing radiation to the skin.

The CTP acquisition protocol at Mass General has always been, and continues to be, well below this epilation threshold, as well as below the 500 mGy limit for CTP dose considered safe by the FDA. As an additional safety precaution, it is department policy at Mass General that CT protocols may not be altered by anyone other than a few senior radiologists within each division, and that the CT scanners are password protected to prevent unauthorized changes in examination settings. In addition, CTP examinations are monitored by a radiologist who determines the correct location for the scan and ensures that the proper scanner protocol is being used.

Our shuttle mode CTP scanning protocol described above results in a radiation exposure, the volumetric CT dose index (CTDIvol), of 349 mGy. Note that this kVp setting is lower than that used for standard CT studies (120-140 kVp), and was selected primarily because the conspicuity of the iodine contrast agent is much greater at 80 kVp than at 140 kVp, resulting in improved CTP map image quality at a markedly lower radiation dose.

CTDIvol reflects the average dose delivered within the scanned volume, and can be measured with a standard head CT dose phantom. The dose length product (DLP) is the CTDIvol multiplied by the length of the scan in cm, and is approximately 2790 mGy-cm for a shuttle mode CTP acquisition. Both the CTDIvol and the DLP are displayed on the CT scanner console. The "effective dose," measured in milli-Sieverts (mSv), is estimated by multiplying the CTDIvol by a conversion factor specific to the radiosensitivity of the scanned region. The effective dose is used to estimate cancer risk to patients. The effective dose for a standard head CT examination at most centers, including Mass General, is 2-3 mSv, and the effective dose for a full shuttle mode brain CTP is approximately 6 mSv. By way of comparison, the annual effective dose per individual in the USA from all sources is approximately 6.2 mSv, of which only 3 mSv can be attributed to medical exposure. The other 3.2 mSv are due to background radiation (3.11 mSv) and consumer products (0.13 mSv). Additional exposure from cosmic rays from living in Denver, Colorado, for one year, rather than at sea level, adds approximately 1.12 mSv to this total. The occupational limit for radiation workers (including radiologists) is 50 mSv/yr. It should be noted, however, that because a comprehensive set of imaging studies during hospitalization for stroke (or vasospasm following aneurysmal subarachnoid hemorrhage) can include multiple serial head CTs, head and/or neck CTAs, and catheter arteriograms, the cumulative radiation dose over a single admission must be a consideration whenever a follow-up CTP study may be clinically indicated, and alternative tests such as MRI or transcranial Doppler ultrasound should be contemplated.
Recommendations

CT perfusion imaging can provide valuable information in emergent settings for acutely ill patients, including those with ischemic stroke and aneurysmal subarachnoid hemorrhage at risk for vasospasm. When determining the need for follow-up CTP exams, however, consideration should be given to the cumulative radiation exposure in a patient cohort likely to receive multiple, serial imaging studies involving ionizing radiation, including fluoroscopy, unenhanced CT, CTA, and CTP.

Figure 2. CT images in a patient with left hemiparesis. Admission CTP images show A) cerebral blood flow (CBF), B) cerebral blood volume (CBV), and C) mean transit time (MTT). The presence of a matched CBF/CBV perfusion deficit suggests irreversibly ischemic infarct "core", likely to correlate with DWI findings, and not a target for reperfusion therapies; D) shows the admission non-contrast CT, and E) shows the final infarct volume on the follow-up CT, which closely matches the admission CBF and CBV lesions (A and B). Depending on the degree of contrast arrival delay downstream from the vascular occlusion (related to both collateral flow and blood pressure), the larger admission MTT lesion (C) may reflect either true "at-risk" ischemic penumbra that has been spared due to early reperfusion, or benign oligemia.
Further Information
For further questions about CT perfusion imaging, please contact Michael H. Lev, MD, at 617-724-7125.

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References


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