Neuroradiology (2012) 54:907–918
DOI 10.1007/s00234-012-1028-6

CONTINUING EDUCATION

The alphabet soup of perfusion CT and MR imaging: terminology revisited and clarified in five questions

Carlos Leiva-Salinas · James M. Provenzale · Kohsuke Kudo · Makoto Sasaki · Max Wintermark

Received: 27 January 2012 / Accepted: 8 March 2012 / Published online: 10 April 2012

Abstract The five questions answered in this article revolve around the different parameters resulting from perfusion imaging processing, and this clarifies the frequently confusing terminology used to describe these parameters. More specifically, the article discusses the different imaging techniques and main mathematical models behind perfusion imaging, reviews the perfusion attributes of brain tissue, and proposes a standardized parameter terminology to facilitate understanding and avoid common misinterpretations.

Keywords Stroke · CT · MRI · Perfusion · Thrombolysis

C. Leiva-Salinas · M. Wintermark
Department of Radiology, Neuroradiology Division,
University of Virginia,
Charlottesville, VA, USA

C. Leiva-Salinas
Department of Radiology, Neuroradiology Division,
Hospital Universitario y Politécnico la Fe,
Valencia, Spain

C. Leiva-Salinas
Department of Medicine, Universidad Autónoma de Barcelona,
Barcelona, Spain

J. M. Provenzale
Department of Radiology, Duke University Medical Center,
Durham, NC, USA

J. M. Provenzale
Departments of Radiology, Oncology and Biomedical Engineering, Emory University School of Medicine,
Atlanta, GA, USA

K. Kudo · M. Sasaki
Division of Ultra-high Field MRI,
Institute for Biomedical Sciences, Iwate Medical University,
Morioka, Japan

M. Wintermark (✉)
Department of Radiology, Neuroradiology Division,
University of Virginia Medical Center,
1215 Lee Street-New Hospital, 1st Floor, Room 1011,
PO Box 800170, Charlottesville, VA 22908, USA
e-mail: Max.Wintermark@virginia.edu

Introduction

The perfusion imaging literature may be confusing at times considering the multiple perfusion imaging techniques [e.g., perfusion-CT (PCT), dynamic susceptibility imaging (DSC), dynamic contrast enhanced, arterial spin labeling (ASL), etc.] (Table 1), the multiple models behind the calculation of the different perfusion parameters (maximal slope method, central volume principle, deconvolution, etc.), and the myriad of perfusion parameters that have been reported [cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), time to peak (TTP), time to maximum (T_{max}), T0, first moment (FMT), full-width half maximum (FWHM), etc.]. To further add to the complexity, various terms have been used to describe the same parameter, and a single term has been used to characterize multiple different concepts.

Through five questions, this article proposes to review and compare the perfusion attributes of brain tissue and to propose a standardized terminology to facilitate understanding and avoid common misinterpretations of perfusion imaging.

What is deconvolution, and is it important?

Deconvolution methods represent a means to correct for a fundamental limitation of perfusion maps, i.e., the influence of the arterial input function (AIF) on the perfusion data. A

Table 1 Overview of the different CT- and MRI-based perfusion imaging techniques

Perfusion technique	Type of tracer employed	Perfusion parameters that may be obtained
CT perfused blood volume (PBV) or MRI bookend method	Iodine-based agents Exogenous Non diffusible	CBV
Dynamic perfusion-CT (PCT)	Iodine-based agents	CBF
	Exogenous	CBV
	Non diffusible	Time parameters
		Parameters describing the blood–brain barrier permeability
Dynamic susceptibility (DSC) perfusion-weighted MR imaging (PWI)	Gadolinium chelates	rCBF
	Exogenous	rCBV
	Non diffusible	Time parameters
Dynamic contrast enhanced (DCE) perfusion-weighted MR imaging (PWI)	Gadolinium chelates	rCBV
	Exogenous Non diffusible	K_{trans}, K_{ep}, V_p, and other parameters describing the blood–brain barrier permeability
Arterial spin labeling (ASL) perfusion-weighted MR imaging (PWI)	Inflowing blood spins Endogenous Diffusible	rCBF

The rows show the different perfusion techniques and the columns illustrate the type of tracer employed and the potential perfusion parameters using each approach

perfusion map is generated from time–concentration curves for each voxel within parenchymal tissue. However, these curves are influenced by two major factors: AIF and the inherent hemodynamic properties of the tissue. Numerous factors can cause alterations in the temporal profile (i.e., AIF) of contrast agent delivery to tissue, resulting in delay, or dispersion, of the contrast bolus. Examples of such factors include impaired cardiac output, carotid artery stenosis, and injection-related factors such as injection rate and saline chase. The resultant alteration in the contrast bolus can cause substantial degradation of the native time–concentration curves within individual voxels. The term deconvolution refers to the mathematical operation that minimizes the effect of the AIF on native time–concentration curves, thereby allowing the true hemodynamic properties of tissue to be depicted [1, 2].

Following data acquisition, perfusion source images are transferred to a postprocessing workstation where software creates parametric maps for perfusion quantification and clinical interpretation, using a mathematical algorithm.

Deconvolution-based models allow calculation of mean capillary network transit time (MTT) and CBF by comparing the shape of the time–concentration curves of the tracer at the arterial input and at the brain tissue of interest [1, 2]. The result of the deconvolution is the tissue residue function, which represents the proportion of contrast material remaining in the voxel over time after arrival of an instantaneous, infinitely short bolus of this contrast material in the voxel. It is actually the determination of the tissue residue function that allows calculation of quantitative information such as the CBF and MTT, even for low injection rates [3] (Fig. 1). Mathematically, the height of the tissue residue function represents the CBF in that voxel. MTT corresponds to the arithmetic mean of the time of transit values represented in the tissue residue function [4] (Fig. 2). These parameters are of vital importance; CBF is the single parameter that best describes the perfusion of a tissue, and MTT is the most appropriate parameter to indicate arterial perfusion pressure decay.

Other perfusion parameters can be calculated directly from the parenchymal time–concentration curves (Table 2, Fig. 3) without deconvolution. However, such parameters are subject to a number of limitations that are not applicable to CBF and MTT when the deconvolution operation is employed. First, as mentioned earlier, inaccuracies can be introduced by alterations of the AIF [5, 6]. However, in addition, the exact physiological meaning of these simpler parameters is difficult to determine.

Deconvolution has two additional advantages compared to other non-deconvolution models to calculate the perfusion attributes. First, it does not rely on simplified assumptions regarding the underlying vascular architecture, assumptions that can result in erroneous values in clinical situations where they are not respected. Second and as mentioned above, it yields quantitative results, even for low rates of contrast material injection. Despite its advantages, the deconvolution method has some disadvantages, such as higher computational demands and more complicated and potentially time-consuming processing of data [1–3]. However, these factors are rendered less relevant given the increasing availability of high speed data processing programs.

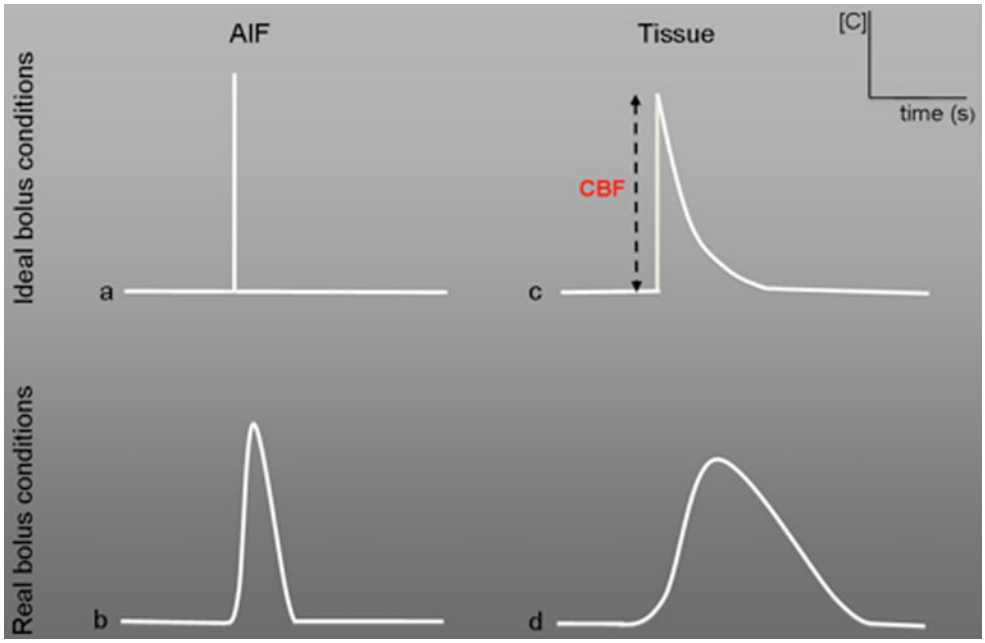

Fig. 1 Figure depicting the concept of deconvolution. Four time–concentration curves are shown, with time (s) depicted on the *x*- axis and tracer concentration [*C*] on the *y*-axis. The *two curves on the left* represent the arterial input functions. The *two curves on the right* show the concentration of tracer in the tissue voxel as a function of time. The *top row* (**a**, **b**) represents an idealized situation, in which an instantaneous, infinitely short bolus of contrast is delivered by the arterial input function (AIF) (**a**) into a voxel of brain parenchyma. In this case, the parenchymal time–concentration curve (**b**) reaches its maximum immediately and then falls gradually as the bolus leaves gradually the voxel via the postcapilary vein. This curve is a "residue function," reflecting the proportion of the tracer remaining in the tissue as a function of time. In this exemplar model, CBF in the considered voxel is equal to the peak of the residue function, i.e., the peak tracer concentration at the time when the bolus arrives in this voxel. The *bottom row* (**c**, **d**) illustrates a more realistic situation as seen in clinical scenarios, in which the tracer is delivered over a brief but not instantaneous period of time, due to bolus delay and dispersion. Both in the AIF (**c**) and in the parenchymal voxels (**d**), the tracer concentration rises and falls more gradually. Computation of CBF in this voxel is more complex than in the scenario depicted in the *top row* because the tracer concentration no longer depends solely on CBF but also on the shape of the AIF. In order to derive the true hemodynamic properties of the voxel under consideration, the effects of the AIF on the tissue concentration curve must be removed using the mathematic operation called "deconvolution," which then provides the value termed the residue function. If the actual AIF and tissue concentration curves are both known, the CBF can be accurately calculated

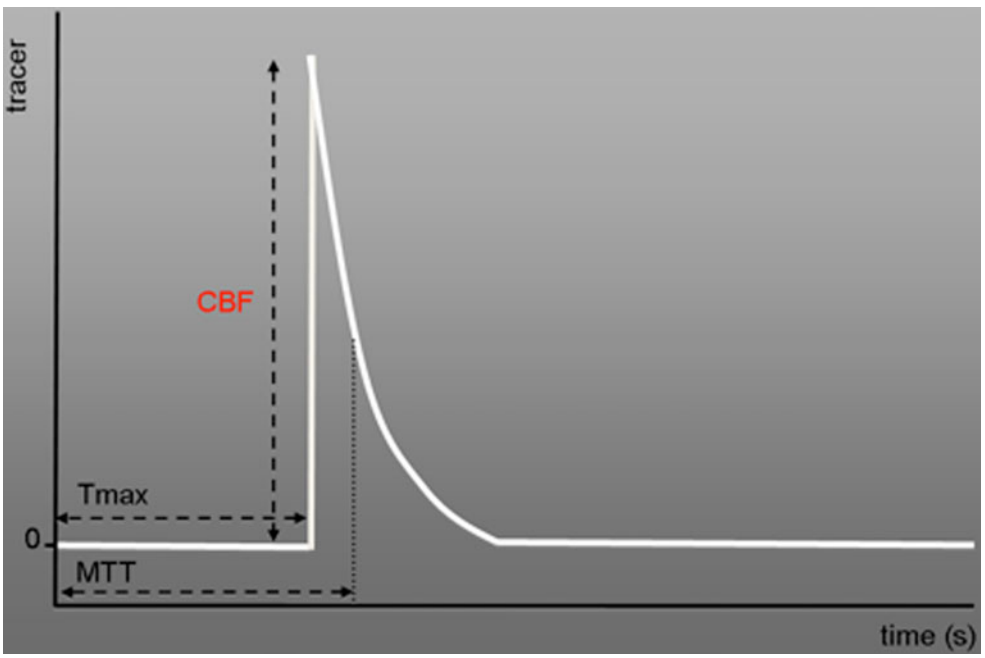

Fig. 2 Perfusion parameters obtained from the tissue residue function calculated by deconvolution. In the graph, time (s) is measured on the *x*- axis and the remaining tracer within the voxel on the *y*-axis. CBF is the peak of the residue function. MTT is the weighted arithmetic mean of the time of transit values represented in the tissue residue function. Tmax is the time-to-maximum of the tissue residue function, i.e., the time to arrival of contrast considering the shape of the tissue residue function

Table 2 Classification of the perfusion parameters based on the physiological information they provide and on the way they are computed/obtained

Physiological/perfusion information	Perfusion parameters obtained from the tissue residue function calculated by deconvolution	Approximation perfusion parameters measured directly from the time-contrast curves, without deconvolution
Volume of blood vessels in the tissue		CBV
Blood flow to the tissue	CBF	Maximal slope
		Cmax
Time it takes for the contrast to traverse the tissue capillary bed	MTT	FWHM
		FMT
		BAT
Delay of the contrast bolus	Tmax	FMT
		BAT
		TTP
		rTTP
		BET

The rows show the physiological information about perfusion that is estimated by each parameter and the columns, whether the parameters are obtained after mathematical calculation or from direct analysis of the observed tissue contrast–time curve

What are the perfusion parameters obtained through deconvolution?

CBF

The term CBF refers to the volume of blood flowing per brain mass for a unit of time, which is measured in the unit milliliters per 100 g per minute. Mathematically, CBF is represented by the peak height of the residue function (Fig. 2). CBF is considered as the single parameter that better reflects the perfusion of a tissue. CBF values are absolute in the case of PCT. The abbreviation rCBF is used when relative CBF values are obtained after deconvolution for DSC MR perfusion weighted imaging (PWI) (please see response to question 5, "Do all perfusion imaging techniques lend themselves to calculation of all parameters?").

MTT

Mean transit time designates the average time required by a bolus of blood to cross the capillary network and is measured in seconds. Mathematically, it corresponds to the weighted arithmetic mean of the time of transit values represented in the tissue residue function (Figs. 2, 4, and 5). MTT is inversely proportional to the cerebral perfusion pressure and is the perfusion parameter that is the most sensitive to hemodynamic disturbances (e.g., ischemia). MTT values are absolute in the case of PCT. However, the term rMTT is used when relative values are obtained for PWI in a manner similar to that of the relative value rCBF.

Of note, the parameters CBF, MTT, and CBV are mathematically related by the equation: CBF = CBV/MTT, which is also known as the central volume principle. Thus, measurement of any two of these parameters is sufficient to derive the third parameter.

T_{max}

The term time-to-maximum (T_{max}) refers to the time to appearance of the maximum level of tissue residue function. Considering the shape of the tissue residue function, it represents the time to arrival of contrast after deconvolution (Figs. 2, 4, and 5). It is an absolute value and expressed in seconds. It is influenced by bolus delay and dispersion [7]. The true physiological meaning of Tmax is elusive and the value should not be assessed in isolation but instead in the context of other parameters such as CBF, CBV, and MTT. [7].

What are the perfusion parameters that can be obtained without deconvolution?

Some parameters can be obtained directly from the parenchymal time–concentration curves and do not require deconvolution. These include CBV, as well as surrogates for MTT [full width at half maximum (FWHM), first moment of transit (FMT), bolus arrival time (BAT), TTP, and bolus end time (BET)], surrogates for CBF [maximal slope of the time–concentration curve (MS)], and surrogates for CBF or CBV [maximal value of the time–concentration curve (Cmax)] (Figs. 3, 4, and 6). These parameters used to be useful when the computational processing associated with deconvolution was time-consuming, which is not longer the case with modern, powerful processors.

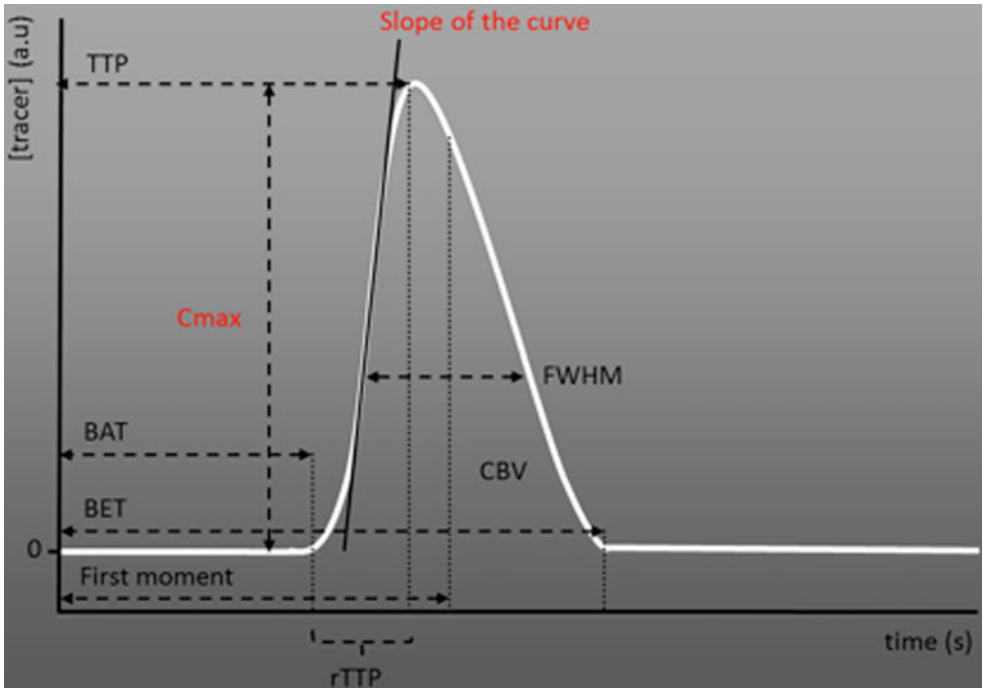

Fig. 3 Perfusion parameters measured directly from the time–contrast curves, without deconvolution. In the graph, time (s) is measured on the *x*-axis and the tracer concentration (arbitrary units) on the *y*-axis. CBV is proportional to the area under the curve of the tissue contrast–time curve. The slope of the curve is the maximal slope of the tissue contrast–time curve. C_{max} is the maximum value of the curve. The bolus arrival time (BAT, or T0) is the time to the arrival of the contrast tracer. Time to peak is the time-to-maximum of the curve. Relative time to peak (rTTP) represents the difference between the TTP and the BAT. Full width at half maximum (FWHM) represents the width of the concentration–time curve when it reaches half of its maximum value. First moment is the weighted arithmetic mean of the time values represented in the time–concentration curve. The bolus end time (BET) is the time to the clearance of the contrast tracer. Estimates of the CBF are displayed in *red* and estimates of the CBV and MTT are in *black*

CBV

The term CBV refers to cerebral blood volume, which is equivalent to the fraction of a voxel that contains blood vessels. It is expressed in the unit milliliter/100 g. CBV calculation from perfusion studies relies on the assumption that the perfusion tracer is confined to the intravascular compartment (and not diffusing into tissue). On a mathematical basis, CBV is proportional to the area under the curve of the time–contrast curve within tissue (Fig. 3). As one might expect, the area under the curve is higher in those voxels containing solely vessels compared to those containing a mixture of vessels and brain parenchyma (in which the vascular volume may represent only a small percentage of the total volume). The resulting partial volume-averaging effect can be used to deduce information regarding the fraction of vascular volume within the total tissue volume and to derive a CBV map. CBV quantification requires knowledge of the contrast enhancement profile in a reference pixel devoid of partial volume-averaging effect (e.g., within a large vein), which can serve as a normalization standard against which voxels containing both vessels and parenchyma can be compared. Such a comparison allows quantification of a regional CBV [1, 2]. In other words, CBV is the volume of distribution of a purely intravascular contrast tracer.

In some situations, the assumption of containment of contrast material within the intravascular compartment is not realized. For instance, in many disease entities (e.g., inflammatory or neoplastic conditions), substantial breakdown of the blood–brain barrier occurs (Fig. 7). Resultant leakage of contrast material into the extravascular space causes an overestimation of the fractional vascular volume and, thus, of the CBV values in PCT studies [8]. Similarly, in DSC PWI studies, the resulting T1 shortening leads to an underestimation of the CBV values [9].

CBV is generally agreed to be the best parameter to assess the size of the core of an infarct and to evaluate the angiogenesis in brain tumors [10, 11]. CBV values are absolute when derived by PCT. The abbreviation rCBV is used when solely relative values are obtained after deconvolution, e.g., in the setting of MR perfusion techniques, such as DSC PWI.

Maximal slope of the time–concentration curve and maximal value of the time–concentration curve

The MS and Cmax parameters are calculated from dynamic imaging without the need for deconvolution. As such, they are

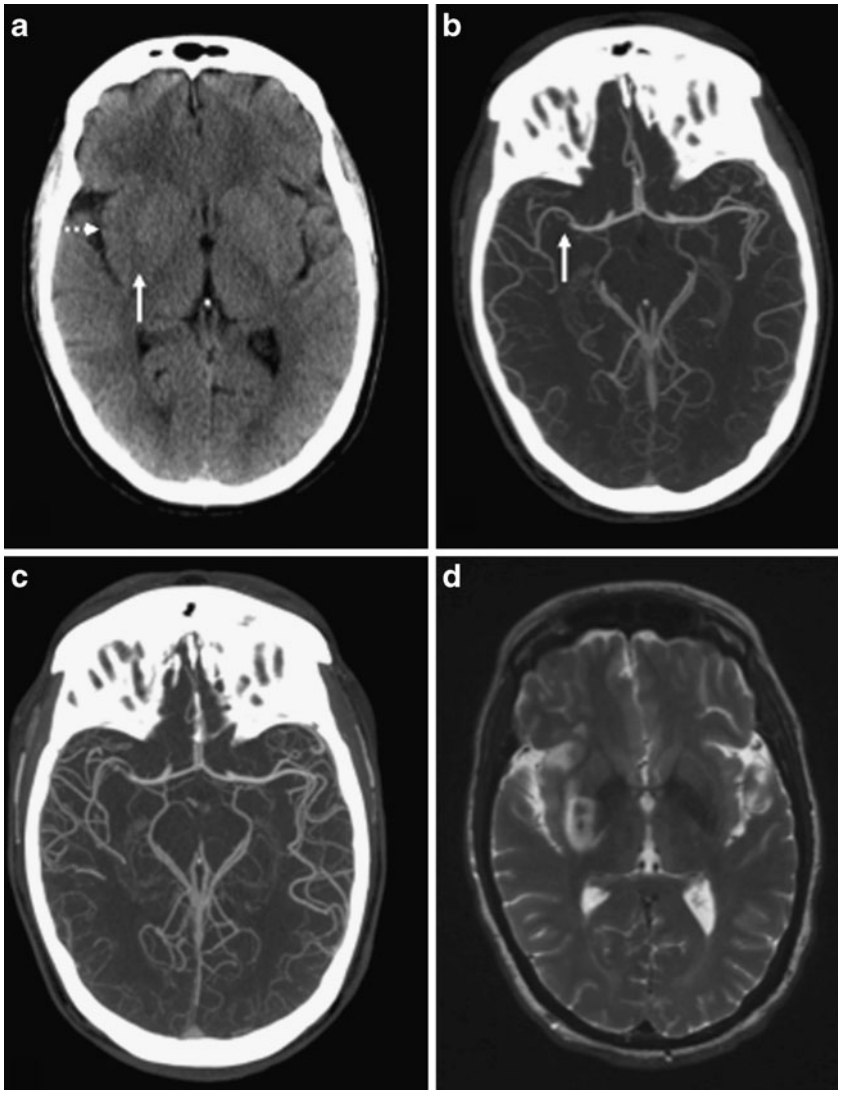

Fig. 4 Serial CT and MR imaging studies of a 61-year-old woman with acute right acute MCA territory infarct successfully treated with iv tPA. **a** Unenhanced CT of the head obtained 3.5 h after symptom onset shows partial obscuration of the right lentiform nucleus (*solid white arrow*) and a subtle loss of gray white differentiation within the right insula (*dotted white arrow*). **b** MIP image from CTA of the intracranial arteries show occlusion of the distal M1 segment of the right middle cerebral artery (*solid white arrow*). **c** Recanalization MIP image of the intracranial arteries performed 24 h after tPA infusion show partial arterial recanalization. **d** Follow-up T2-weighted MR image obtained 4 days after symptom onset show final infarct volume as well as hemorrhagic transformation

both imperfect surrogates of CBF because neither of them is quantitative and can only be used as relative values. Although parameters based on deconvolution methods are preferred, these parameters can be used when deconvolution-based software is not available.

The MS parameter represents the wash-in of the tracer bolus. A steep slope denotes a rapid arrival of tracer to the tissue and therefore correlated with, in general, a greater CBF [6]. However, this estimation of CBF is not straightforward because the slope of the contrast–time curve is influenced not only by CBF but also by the rate the tracer is delivered to the tissue through the AIF [6]. CBF values calculated using the maximal slope model are underestimated [2] (Fig. 3).

Cmax represents the maximal value of the tissue time–concentration curve recorded during dynamic imaging. Cmax is an estimate of the CBF, but it is not as robust as the CBF calculated using deconvolution methods because it is influenced by MTT (Fig. 3).

FWHM, FMT, BAT, TTP, and BET

The following parameters are less commonly used than CBF, CBV, and MTT and are calculated from dynamic imaging without deconvolution. They are all imperfect surrogates of MTT because they are strongly influenced by those factors to which PCT is made vulnerable in the absence of deconvolution, such as bolus delay or dispersion, reduced CBF, prolonged MTT, or any combination of these factors. As a result, they should be used only when deconvolution-based software is not available. When available, deconvolution MTT should be preferred.

FWHM stands for full width at half maximum and is measured in seconds. FWHM represents the width of the time–signal curve when it reaches half of its maximum value (Fig. 3).

FMT stands for first moment of transit and is expressed in seconds. FMT is the weighted arithmetic mean of the time values represented in the time–concentration curve (as MTT

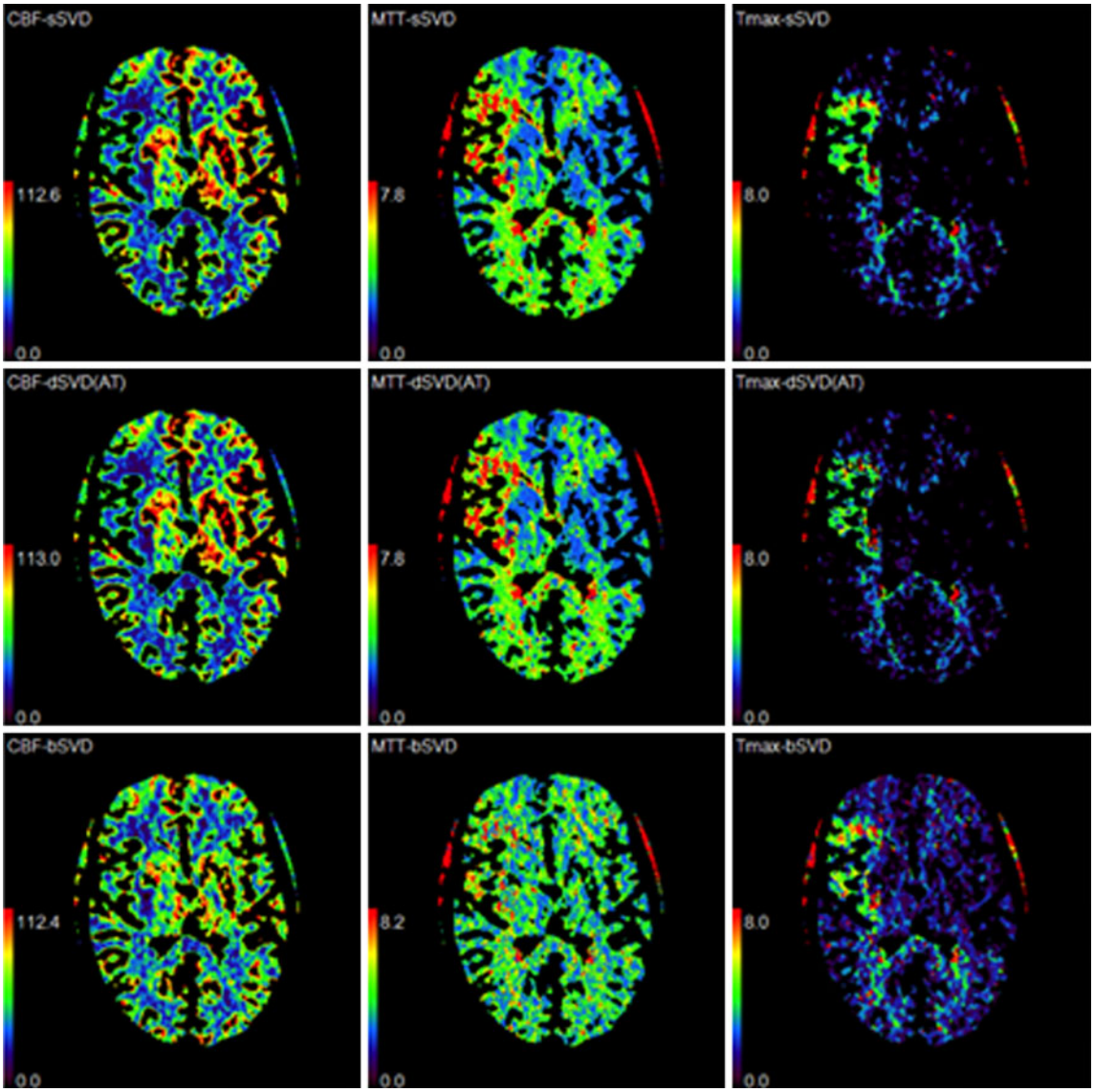

Fig. 5 Baseline perfusion parametric maps processed using different deconvolution algorithms for the same patient as in Fig. 4. *First row* shows CBF, MTT, and Tmax maps calculated using standard singular value decomposition (sSVD). *Second row* shows CBF, MTT, and Tmax maps processed using bolus arrival time delay-corrected single value decomposition [dSVD(AT)]. *Third row* shows CBF, MTT, and Tmax maps calculated using block-circulant single value decomposition (bSVD). Color scales are shown in the *lower left corner* for each parametric map; *red* represents high values and *blue* low values. The area of predicted ischemic penumbra as represented by the area of prolonged MTT or Tmax (*depicted in red*) differs somewhat depending on the algorithm employed

is the weighted arithmetic mean of the time values represented in the tissue residue function) (Fig. 3).

BAT, or bolus arrival time, describes the time to the arrival of the contrast tracer as obtained from the time–signal curves and is thus a measure of the delay of the bolus (Fig. 3). It is expressed in seconds.

BET, or bolus end-time, indicates the time to the clearance of the contrast tracer as obtained from the time-signal curves (Fig. 3). It is expressed in seconds.

TTP stands for time-to-peak, i.e., the time to the maximum point of the time-signal curve and is expressed in seconds (Fig. 3). It represents the time at which the maximum change in tracer concentration occurs after the passage of the bolus [12]. Thus, the terms Tmax and TTP appear to be very similar, a fact that is further explained in the following section.

Can the terms "Tmax" and "TTP" be used interchangeably?

Although Tmax and TTP are similar in some ways, they represent distinct entities and cannot be used interchangeably. TTP refers to the time-to-peak of the tissue time–signal curve (Fig. 3), which can be obtained without the

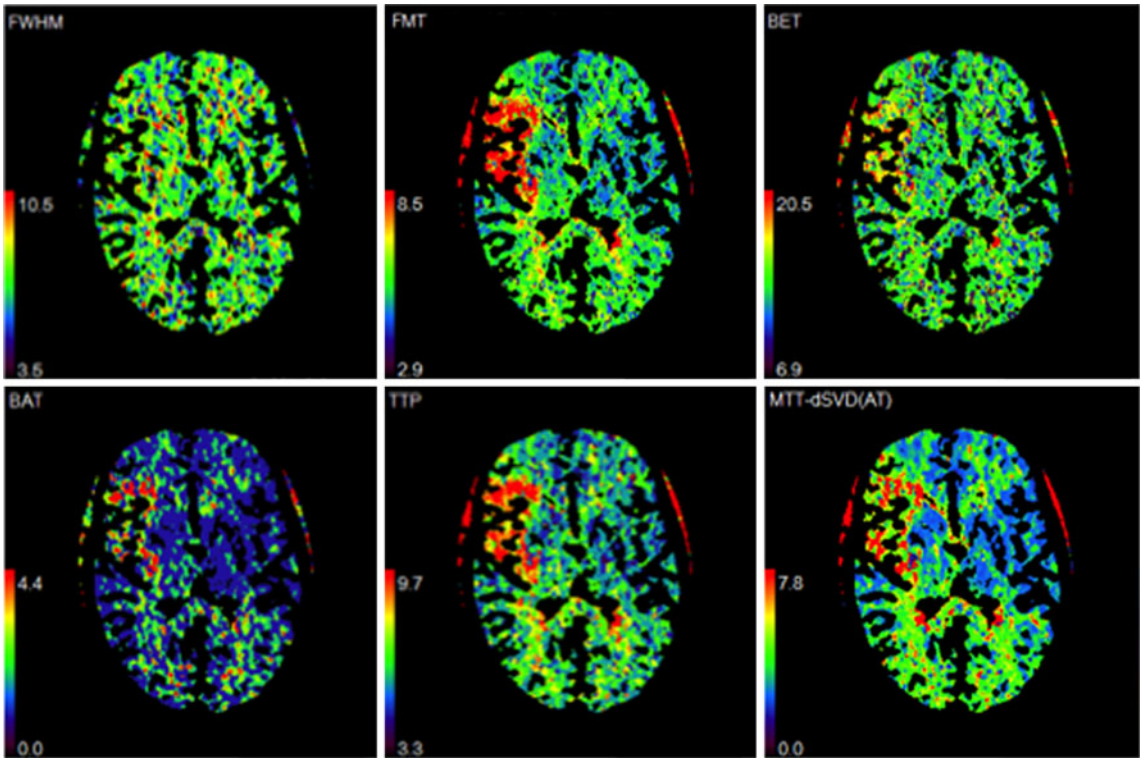

Fig. 6 Baseline basic time perfusion parametric maps obtained without deconvolution for the same patient as in Figs. 4 and 5. *FWHM* full width at half maximum, *FMT* first moment of transit, *BAT* bolus arrival time, *TTP* time to peak, *BET* bolus end time. Numerous time parameters can be obtained without deconvolution. These parameters show an abnormal region that can either be very similar or quite different from the one demonstrated by the deconvolution MTT map

deconvolution process. On the other hand, Tmax is the "time-to-peak" of the residue function which can solely be obtained after deconvolution.

In an analogous fashion, similarities exist between FMT (i.e., the first moment of transit) and MTT (mean transit time). However, FMT is the first moment of the tissue time–signal curve, which can be generated without the need for the deconvolution process. On the other hand, MTT is the first moment of the residue function that can solely be obtained after deconvolution.

The similarities between terms have occasionally led to them being confused with one another in the medical literature. For instance, the TTP acronym has alternately been employed to describe the time to maximum contrast concentration obtained from the time–contrast curve and the time to maximum contrast concentration minus the bolus arrival time obtained from the time–contrast curve [5, 6, 12–14]. In a similar vein, the MTT acronym has not only been employed to (appropriately) refer to the MTT obtained from deconvolution but also inappropriately used to refer to the full width half maximum (FWHM).

Just as similar terms have been used to incorrectly indicate the same parameter, so too have various terms have been used to refer to the same entity. For instance, the terms "time of contrast arrival," "bolus arrival time," "arrival time fitted," or "T0" all have been used to refer to the same condition, i.e., the delay in arrival of contrast material in a voxel obtained from the time–contrast curve.

A standardized terminology to describe the different parameters that describe perfusion attributes is proposed in Table 3. Use of this table would be expected to help the reader avoid common misinterpretations and facilitate understanding of perfusion imaging.

There are two types of deconvolution, delay-sensitive and delay-corrected. What is the difference between these two types, does it matter, and which type of deconvolution should you use?

One of the fundamental assumptions for applying the deconvolution process is that the AIF is measured directly at the inlet of the tissue, i.e., no delay exists between the arrival of the contrast agent bolus at the site where the AIF is measured and the brain voxel [15–19]. In practice, however, the AIF must be obtained from an artery (usually one of the branches of the anterior or middle cerebral artery) rather than a small arteriole located very close to the tissue of interest. By necessity, some distance must exist between the artery serving as the source of the AIF and the tissue it supplies. Depending on

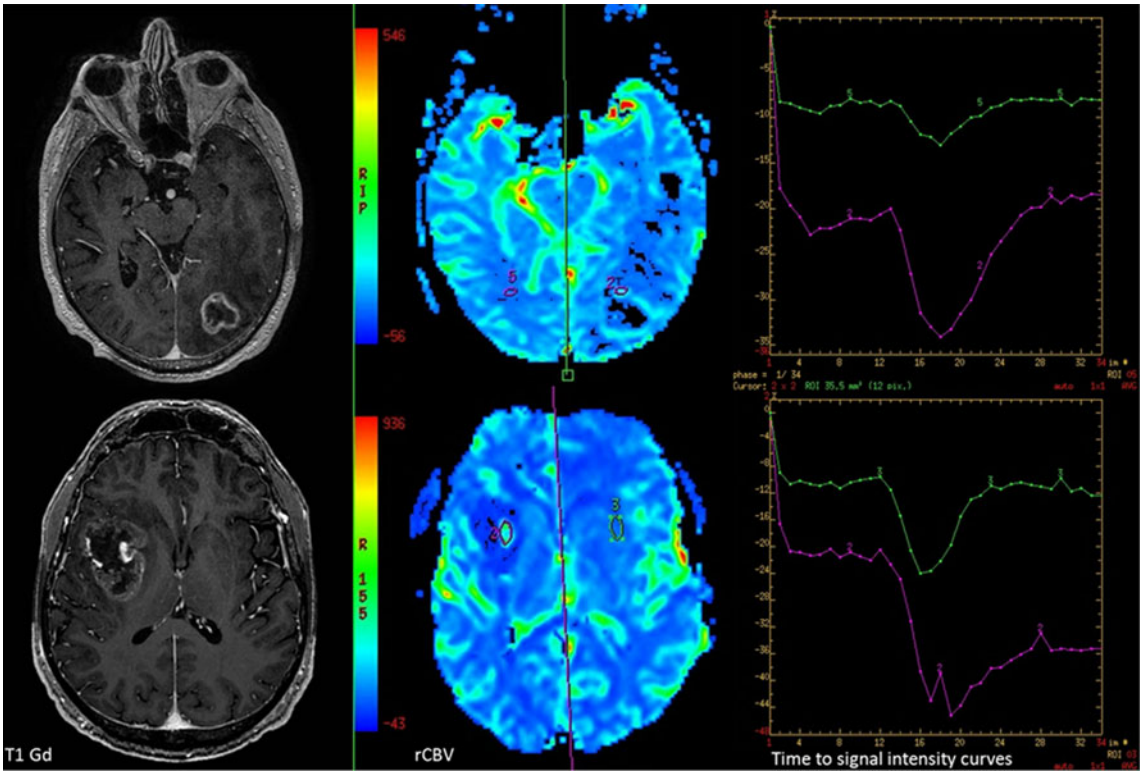

Fig. 7 Brain tumor characterization using perfusion-weighted MRI. Contrast-enhanced T1-weighted images, perfusion-weighted rCBV maps and corresponding T2* susceptibility time-signal intensity curves in a 57-year-old female patient with a left occipital glioblastoma multiforme (GBM) (top row) and a 62-year-old male patient with a single frontal metastasis from an urothelial carcinoma (*bottom row*). Enhancing portion of both lesions shows an increased rCBV, featured as an increased area over the time–intensity curves. The two types of lesions demonstrate a marked difference in terms of the signal intensity recovery at the end of the first pass. GBM has an almost complete signal intensity recovery to the baseline, while the metastasis has a poor return to baseline. Capillaries of metastatic brain tumor resemble those of systemic origin instead of those present in healthy brain tissue; they are devoid of any rudimentary BBB architecture and are highly permeable to gadolinium, explaining the poor return to baseline. GBM microvasculature is composed of newly formed capillary buds that, nevertheless, retain some BBB, explaining the preserved return to baseline

local vascular factors, e.g., stenoses, a delay can occur so that the arrival of the bolus at the site of AIF placement and the arrival at the tissue of interest are not simultaneous.

The deconvolution operation can be performed according to different methods. The classical deconvolution method is termed "standard singular value decomposition" (sSVD). This technique is robust and independent of the underlying vascular structure. However, the technique is delay-sensitive; when a delay occurs, MTT is overestimated and CBF is underestimated [20]. The use of the such falsely abnormal CBF/MTT values may lead to overestimation of the ischemic penumbra by including brain regions that just present a delay in the contrast agent arrival but are not truly ischemic [17]

To overcome these difficulties, new deconvolution methods have been developed to minimize the effects of bolus delay and dispersion [16, 19]. In "delay-corrected" deconvolution (dSVD), the delay in contrast agent arrival between the AIF and the brain tissue is corrected by shifting in time the arterial and parenchymal time–concentration curves so that the beginning in the concentration rise is synchronous for all curves [16]. This method yields more stable results than the sSVD regardless of the contrast agent delay. It has been applied successfully in perfusion-weighted MRI [21]. However, correct application of this process depends on accurate estimation of the delay, which is difficult on perfusion CT due to the relatively poor contrast-to-noise ratio [16].

Yet another novel delay-insensitive technique is the block-circulant deconvolution (bSVD or cSVD or o SVD) algorithm [19]. This approach removes the causality assumption that is part of standard deconvolution algorithm, i.e., that the tracer cannot arrive at the tissue voxel earlier than it arrives in the AIF. In practice, however, the selected AIF is not necessarily the true AIF for that voxel. Thus, tracer arrival in the tissue of interest can actually precede the arrival time in the AIF that has been selected, as, for instance, when the AIF is selected from a severely stenotic or obstructed vessel [16, 19]. This method has been shown to be remarkably insensitive to circulatory delay when evaluated in phantoms and patients with stroke, both using CT or MR approaches [16, 19]. Moreover, it is equivalent to the standard deconvolution technique when there is no delay between the tracer arrival in the AIF and the tissue [19]. In

Table 3 Overview of the perfusion parameters that can be obtained from the time–concentration curve

Standardized terminology	Significance	Other used terms to describe the same concept
Mean transit time (MTT)	Average time required by a bolus of blood to cross the capillary network—*requires deconvolution*	
Cerebral blood flow (CBF)	Volume of blood flowing per brain mass for a unit of time—*requires deconvolution*	
Cerebral blood volume (CBV)	Area under the curve	Area under the curve
		Negative integral enhancement
Maximal slope (MS)	Maximal slope of the curve	
Cmax	Maximal value of the curve	Peak height
Full width half maximum (FWHM)	Width of the curve when it reaches half of its maximum value	
First moment of transit (FMT)	Weighted arithmetic mean of the time values represented in the curve	
(Bolus arrival time) BAT	Time to the arrival of the contrast tracer in the curve	Time of contrast arrival
		Arrival time fitted
		Time to start (TTS)
		T0
Time-to-peak (TTP)	Time-to-maximum of the curve	Peak time fitted
Bolus end time (BET)	Time to the clearance of the contrast tracer obtained from the curve	Time to drain (TTD)

some studies, it has been considered the "gold standard" to which compare the rest of methods [15].

It is important for radiologists using CT and MRI perfusion imaging for assessment of stroke patients to be aware of whether the analysis program in use at their institution is deconvolution based and, if so, whether the deconvolution method is delay-sensitive (which can have a dramatic influence on the results). To minimize the possibility of inaccurate results, the radiologist should always review the CTA images acquired in conjunction with CT perfusion imaging in order to detect possible arterial stenoses or occlusions that may cause delay or dispersion of the bolus of contrast material. In such situations, the AIF selection can have a significant impact on MTT and CBF calculation (Fig. 4). For instance, when using software based on a delay-sensitive deconvolution approach, a delay in transit of contrast material due to a hemodynamically significant carotid stenosis can cause falsely prolonged MTT values in the territory supplied by the stenotic artery (Fig. 2). In this case, the time–signal curve of each vascular territory can be deconvolved by an AIF derived from its own specific parent artery. On the other hand, when using delay-insensitive bSVD-based software, one must be aware that the CBF values may be slightly erroneous when the bolus arrives in the tissue before the AIF. Therefore, in theory, for research purposes, selecting the AIF in the healthy, non-ischemic hemisphere would be recommended to obtain reliable quantitative results when using such an approach [16]. This effect is so minimal that, in practice, selecting the ACA as the AIF has no real influence on the accuracy of the CBF values.

As a general rule, the use of a delay-insensitive method is recommended when dealing with stroke patients, a population in which arterial stenoses are common.

Do all perfusion imaging techniques lend themselves to calculation of all parameters?

Not all perfusion techniques give information about each of the perfusion parameters. The type of contrast tracer, the acquisition mode and the physical principles behind each perfusion technique determine their capabilities, strengths and limitations for the estimation of the perfusion attributes.

As stated earlier, CBV describes the volume of distribution of a purely intravascular contrast tracer. It is evident that perfusion techniques that use non-diffusible tracers are very good at CBV calculation while techniques that use diffusible tracers, such as ASL, may not accurately determine CBV.

Perfusion techniques that are based on a dynamic acquisition, i.e., use first-pass tracer methodology after intravenous injection of a rapid bolus of contrast material, allow for the calculation of CBV, CBF, and time parameters. Conversely, techniques that use a static acquisition, such as CT perfused blood volume (PBV), can only determine CBV but cannot provide accurate measurements of time parameters or CBF.

Finally, on MR perfusion imaging, the relationship between the T1 signal increase or the T2/T2* signal decrease and concentration of gadolinium contrast agent is not linear. Thus, analysis of the changes in signal intensity (i.e., the time–signal intensity curves) does not afford qualitative

estimation of local concentrations of contrast material. Thereby, DSC or DCE PWI does not provide quantitative information about brain perfusion but solely semiquantitative comparison of one hemisphere to the other [2]. For this reason, only relative, and not absolute values of CBF and MTT can be provided.

Table 1 offers an overview of the different techniques and the perfusion parameters that may be obtained with each one.

Conclusion

In this review, we have acquainted the reader with the meaning of various terms used in perfusion imaging as well as explained how the choice of data analysis technique influences the parameters that can be accurately measured, i.e., which sequence of letters in the alphabet soup are available. Radiologists should be familiar with the different imaging techniques available to assess brain perfusion and the information they can provide. The knowledge of the different mathematical models for perfusion characterization at one's institution is also vitally important since choice of technique has a direct impact on the quality and reliability of the parametric maps. Finally, a better understanding of the terminology for the parameters that describe brain perfusion may, hopefully, avoid confusion and facilitate comparisons when analyzing research studies involving perfusion techniques.

Key Learning Points

- The perfusion imaging literature may be confusing at times considering the multiple perfusion imaging techniques, the multiple models behind the calculation of the different perfusion parameters, and the myriad of perfusion parameters that have been reported.
- Radiologists should be familiar with the different imaging techniques available to assess brain perfusion and the information they can provide and more specifically with the method they are using at their own institution.
- It is critical to know whether one's perfusion processing software uses devonvolution or not.
- Software that does not use deconvolution is subject to pitfalls related to alterations in the temporal profile of contrast agent delivery to tissue, resulting in delay, or dispersion, of the contrast bolus.
- There are different deconvolution methods currently available, some delay-sensitive and some delay-insensitive. Whether one type of deconvolution is superior to the other is still an active area of research.

Conflict of interest We declare that we have no conflict of interest.

References

1. Konstas AA, Goldmakher GV, Lee TY, Lev MH (2009) Theoretic basis and technical implementations of CT perfusion in acute ischemic stroke, part 2: technical implementations. AJNR Am J Neuroradiol 30:885–892
2. Wintermark M, Maeder P, Thiran JP, Schnyder P, Meuli R (2001) Quantitative assessment of regional cerebral blood flows by perfusion CT studies at low injection rates: a critical review of the underlying theoretical models. Eur Radiol 11:1220–1230
3. Eastwood JD, Provenzale JM, Hurwitz LM, Lee TY (2001) Practical injection-rate CT perfusion imaging: deconvolution-derived hemodynamics in a case of stroke. Neuroradiology 43:223–226
4. Copen WA, Sorensen AG (2003) Perfusion-weighted MRI in Stroke. In: Davis S, Fisher M, Warach S (eds) Magnetic resonance imaging in stroke, 1st edn. Cambridge University Press, Cambridge, pp 147–159
5. Kane I, Carpenter T, Chappell F et al (2007) Comparison of 10 different magnetic resonance perfusion imaging processing methods in acute ischemic stroke: effect on lesion size, proportion of patients with diffusion/perfusion mismatch, clinical scores, and radiologic outcomes. Stroke 38:3158–3164
6. Schaefer P, Copen WA, Gonzalez RG (2006) Perfusion MRI of acute stroke. In: Gonzalez RG, Hirsch JA, Koroshetz WJ, Lev MH, Schaefer P (eds) Acute ischemic stroke imaging and intervention. Springer, Berlin, pp 173–197
7. Calamante F, Christensen S, Desmond PM, Ostergaard L, Davis SM, Connelly A (2010) The physiological significance of the time-to-maximum (Tmax) parameter in perfusion MRI. Stroke 41:1169–1174
8. Roberts HC, Roberts TP, Brasch RC, Dillon WP (2000) Quantitative measurement of microvascular permeability in human brain tumors achieved using dynamic contrast-enhanced MR imaging: correlation with histologic grade. AJNR Am J Neuroradiol 21:891–899
9. Lev MH, Rosen BR (1999) Clinical applications of intracranial perfusion MR imaging. Neuroimaging Clin N Am 9:309–331
10. Lacerda S, Law M (2009) Magnetic resonance perfusion and permeability imaging in brain tumors. Neuroimaging Clin N Am 19:527–557
11. Wintermark M, Flanders AE, Velthuis B et al (2006) Perfusion-CT assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. Stroke 37:979–985
12. Sobesky J, Zaro Weber O, Lehnhardt FG et al (2004) Which time-to-peak threshold best identifies penumbral flow? A comparison of perfusion-weighted magnetic resonance imaging and positron emission tomography in acute ischemic stroke. Stroke 35:2843–2847
13. Yamada K, Wu O, Gonzalez RG et al (2002) Magnetic resonance perfusion-weighted imaging of acute cerebral infarction: effect of the calculation methods and underlying vasculopathy. Stroke 33:87–94
14. Grandin CB, Duprez TP, Smith AM et al (2002) Which MR-derived perfusion parameters are the best predictors of infarct growth in hyperacute stroke? Comparative study between relative and quantitative measurements. Radiology 223:361–370
15. Kudo K, Sasaki M, Yamada K et al (2010) Differences in CT perfusion maps generated by different commercial software: quantitative analysis by using identical source data of acute stroke patients. Radiology 254:200–209

16. Kudo K, Sasaki M, Ogasawara K, Terae S, Ehara S, Shirato H (2009) Difference in tracer delay-induced effect among deconvolution algorithms in CT perfusion analysis: quantitative evaluation with digital phantoms. Radiology 251:241–249
17. Konstas AA, Lev MH (2010) CT perfusion imaging of acute stroke: the need for arrival time, delay insensitive, and standardized post-processing algorithms? Radiology 254:22–25
18. Sourbron S (2010) Technical aspects of MR perfusion. Eur J Radiol 3:304–313
19. Wu O, Ostergaard L, Weisskoff RM, Benner T, Rosen BR, Sorensen AG (2003) Tracer arrival timing-insensitive technique for estimating flow in MR perfusion-weighted imaging using singular value decomposition with a block-circulant deconvolution matrix. Magn Reson Med 50:164–174
20. Ostergaard L, Weisskoff RM, Chesler DA, Gyldensted C, Rosen BR (1996) High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. Part I: mathematical approach and statistical analysis. Magn Reson Med 36:715–725
21. Ibaraki M, Shimosegawa E, Toyoshima H, Takahashi K, Miura S, Kanno I (2005) Tracer delay correction of cerebral blood flow with dynamic susceptibility contrast-enhanced MRI. J Cereb Blood Flow Metab 25:378–390