Influence of the Arterial Input Function on Absolute and Relative Perfusion-Weighted Imaging Penumbral Flow Detection

A Validation With $^{15}$O-Water Positron Emission Tomography

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Background and Purpose—Perfusion-weighted imaging maps are used to identify critical hypoperfusion in acute stroke. However, quantification of perfusion may depend on the choice of the arterial input function (AIF). Using quantitative positron emission tomography we evaluated the influence of the AIF location on maps of absolute and relative perfusion-weighted imaging to detect penumbral flow (PF; <20 mL/100 g/min on positron emission tomography $\text{CBF}_{\text{AIF}}$) in acute stroke.

Methods—In 22 patients with acute stroke the AIF was placed at 7 sites (M1, M2, M3 ipsi- and contralateral and internal carotid artery–M1 contralateral to the infarct). Comparative $^{15}$O-water positron emission tomography and AIF-dependent perfusion-weighted imaging (cerebral blood flow, cerebral blood volume, mean transit time, and time to maximum) were performed. A receiver operating characteristic curve analysis described the threshold independent performance (area under the curve) of the perfusion-weighted maps for all 7 AIF locations and identified the best AIF-dependent absolute and relative thresholds to identify PF. These results were compared with AIF-independent time-to-peak maps.

Results—Quantitative perfusion-weighted imaging maps of cerebral blood flow and time to maximum performed best. For PF detection, AIF placement did significantly influence absolute PF thresholds. However, AIF placement did not influence (1) the threshold independent performance; and (2) the relative PF thresholds. AIF placement in the proximal segment of the contralateral middle cerebral artery (cM1) was preferable for quantification.

Conclusions—AIF-based maps of cerebral blood flow and time to maximum were most accurate to detect the PF threshold. The AIF placement significantly altered absolute PF thresholds and showed best agreement with positron emission tomography for the cM1 segment. The performance of relative PF thresholds, however, was not AIF location-dependent and might be along with AIF-independent time-to-peak maps, more suitable than absolute PF thresholds in acute stroke if detailed postprocessing is not feasible. (Stroke. 2012;43:378-385.)

Key Words: acute stroke ■ arterial input function ■ cerebral blood flow ■ cerebral ischemia ■ penumbra ■ perfusion-weighted magnet resonance imaging ■ positron emission tomography

D etecting and rescuing the ischemic penumbra is the main target of acute stroke therapy. In clinical studies, diffusion-weighted and perfusion-weighted (PW) MRIs are used to estimate the tissue at risk. The area of critical ischemia (<12 mL/100 g/min) is represented by the diffusion-weighted imaging lesion and the mismatch volume is estimated by the volumetric difference of the PW penumbral flow threshold <20 mL/100 g/min minus the diffusion-weighted imaging lesion. This volume, the mismatch, may serve as a surrogate of penumbra keeping in mind several methodical restrictions. However, adequate quantification of PW blood flow measures is an ongoing challenge.

A method for absolute and relative thresholding of PWI is extremely important because mild disturbances in perfusion do not result in brain infarction. To this end, many attempts have been made to perform absolute measurements of perfusion parameters and to find absolute or relative threshold values that will help to predict tissue viability and therefore the likely infarct growth. PW maps are supposed to yield absolute perfusion values but suffer from methodical drawbacks. In clinical routine, standard singular value decom-position is commonly used to determine PW-cerebral blood flow (CBF), -cerebral blood volume (CBV), -mean transit time (MTT), and -time to maximum (Tmax) by deconvolu-

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tion of the measured tissue tracer concentration time curve
with the arterial input function (AIF). Thus, the accuracy of
quantitative PW maps may depend mainly on the correct
placement of the AIF, which still has to be defined.8–12
Because the choice of the AIF may cause variability of
resulting absolute and relative perfusion values, this method
must be validated by a reference method for quantitative
perfusion imaging, for example,15O-water positron emission
tomography (PET). In contrast to previous studies that
analyze the influence of the AIF shape on PWI maps8 or
correct for confounding factors of the AIF,13 the current
clinical study focuses on AIF location-dependent penumbral
flow (PF) threshold detection (without sophisticated AIF
corrections). Our AIF-dependent thresholds can be used by
the stroke clinician to improve MR-based treatment decisions
in the acute stroke setting.

In a comparative PET-MRI data set of patients with acute
stroke, we therefore (1) investigate the interobserver reliabil-
ity of the AIF-dependent PW maps; and (2) we define the
optimal placement of the AIF and, to this end, establish the
AIF-dependent best PF thresholds as well as the threshold-
independent PWI map performance to detect the PF threshold
for absolute and relative measures as defined by PETCBF <20
mL/100 g/min.

Materials and Methods

Patients

The presented data contain a subset of a prospective imaging study
of patients with acute and subacute ischemic hemispheric stroke.
Small vessel strokes and pure subcortical strokes were excluded. Part
of this patient population and the inclusion criteria have been
described in previous publications by our group.1,6 All patients gave
informed consent and the study was approved by the local
ethics committee.

MRI and PET

Data acquisition and postprocessing have been described in detail in
a recent study.14 In brief, MRI was performed on a 1.5-T whole-body
scanner (Philips Intera Master, Best, The Netherlands). PW images
were acquired using gradient-echo echoplanar imaging sequences (repetition
time, 1.3 seconds; effective echo time, 25 ms; 20 slices; slice thickness,
6 mm; interslice gap, 0.6 mm; field of view, 23 cm). PET was
performed in a resting state on an ECAT EXACT HR Scanner
(Siemens/CTI). CBF was acquired in a 2-dimensional mode provid-
ing 47 contiguous 3-mm slices of 5-mm full-width half-maximum in
plane-reconstructed resolution. After intravenous bolus injection of
15O-water (60 mCi=2.2 GBq), the tracer distribution was measured
for 90 seconds. Continuous arterial blood sampling was used to
calculate absolute CBF values.

Data Postprocessing and AIF Selection

The postprocessing of the PW raw images was performed by
STROKETOOL, Version 2.3 (DIS) on a pixel-by-pixel basis to
generate quantitative maps of CBF, CBV, MTT, and Tmax from the
tissue-response curve using the nonparametric standard singular
value decomposition.15 The AIF, used for deconvolution, was
defined manually by 2 experienced raters (O.Z.-W., J.S.). Each AIF
is calculated as an average AIF from 2 to 3 different voxel locations
within each segment. The resulting input functions were visually
inspected for peak sharpness, amplitude width, and bolus peak time
to select only nondistorted bolus curves.10 For every patient, the AIF
was derived from 6 different locations within the middle cerebral
artery (MCA): M1, M2, and M3 segment ipsilateral (i) and contralat-
eral (c) to the infarct (iM1AIF, iM2AIF, iM3AIF, cM1AIF, cM2AIF,
cM3 AIF; Figure 1). In line with previous studies6,16 we also included
an AIF derived from the contralateral distal internal carotid artery
and cM1 segments. For each patient, 7 maps for each PW modality
were generated according to the AIF placement. PF thresholds were

Figure 1. PWI raw images with exemplary selection of voxels for the AIF determination (white; n=2) within the M1, M2, and M3 seg-
ments of the MCA in 1 patient (upper images) with the resulting AIFs (beneath). The time intensity curve is shown over time (scans).
ICA voxels not shown. PWI indicates perfusion-weighted imaging; AIF, arterial input function; MCA, middle cerebral artery; ICA, internal
carotid artery.
given as absolute (ie, mL/100 g/min) or as relative measures. The latter was calculated as a ratio to the mean value of all cortical regions of interest of the unaffected hemisphere (see "Image Analysis") for relCBF, relCBV and relMTT (eg, CBF\textsubscript{affected}/CBF\textsubscript{unaffected}), and as a delay to the mean value of all cortical regions of interest of the unaffected hemisphere for relTmax (ie, Tmax\textsubscript{affected}/Tmax\textsubscript{unaffected}) in line with previous studies. We also generated AIF-independent PW maps of time to peak (TTP) to compare its performance with the AIF-dependent measures.

**Image Analysis**

Image analysis was performed by a multimodal imaging tool (VINCI; Max Planck Institute for Neurological Research, Cologne, Germany). PET images were resized to the MR images and then realigned by an automated observer-independent algorithm. For every patient, a 3-dimensional brain mask, created by the individual T1 image, was used to exclude the ventricles, most of the periventricular white matter, large vessels, and the sinuses. Within this individual atlas, the region of interest analysis of the MRI and PET images was performed by 10-mm circular cortical regions of interest in the affected and unaffected hemisphere (Figure 2). For each patient, the set of regions of interest was then copied onto the coregistered PET-CBF images and corresponding PW maps (7 maps for CBF, CBV, MTT, and Tmax, respectively; 28 PW maps in total) as well as on the AIF-independent TTP map. The mean region of interest values were used for further analysis. Voxels within the hypoperfused tissue without contrast bolus arrival were excluded from further analysis.6

**Receiver Operating Characteristic Curve Analysis**

The accuracy of the PW maps to detect hypoperfusion was determined by a receiver operating characteristic (ROC) curve analysis. We used PET to define the area of PF defined by CBF values ≤20 mL/100 g/min. In a first step, the ROC curve analysis was performed for every patient separately. In a second step, the area under the ROC curve (AUC) for each PW map was identified. The AUC represents the performance of PW maps to detect the PF independently from the selected cutoff value. The closer the AUC is to 1, the better the PW map performs. In a third step, the best PF threshold for quantitative (qCBF, qCBV, qMTT, qTmax) and relative (relCBF, relCBV, relMTT, relTmax) PW maps was defined for each patient by the equal sensitivity and specificity threshold. This point was selected because it weights false-positive and false-negative errors equally. The median and interquartile range of these individual PF thresholds as well as their sensitivity and specificity values were calculated in a pooled analysis.

**Influence of Stenosis and Time of Imaging**

To test for the effects of internal cerebral artery (ICA) stenosis and time point of imaging, patients were (1) divided in 2 groups according to the presence or absence of ipsilateral vessel pathology;
and (2) dichotomized according to the time of imaging after stroke onset (cutoff: 24 hours).

**Interobserver Reliability**

Two raters (O.Z.-W., J.S.) independently measured AIFs to assess interobserver reliability. The absolute PW-based CBF values (as well as CBV, MTT, and Tmax values) obtained by each rater for the 7 different AIF locations were compared and the intraclass correlation coefficients were calculated for each location.

**Statistics**

Because most of the study values were not normally distributed, the results were presented as median and interquartile range if not indicated otherwise. The interrater reliability of AIF-dependent PW values was assessed by the intraclass correlation coefficient. Group differences (stenosis, time point of imaging) were calculated by the Mann-Whitney U rank sum test. We tested for differences (AUC, relative and quantiative PF thresholds) between AIF-dependent PW maps using the nonparametric Friedman test. Pairwise comparisons were performed by the nonparametric Wilcoxon signed-rank test to determine significant differences. Statistical significance was set at P < 0.05. Data were analyzed by SigmaPlot 12 (SYSTAT Software) and MedCalc Software (Version 11.6).

**Results**

**Clinical Data**

Of the 22 patients (median age, 56.5 years), 15 were imaged within 24 hours after stroke (median, 9.2 hours) and 7 were measured beyond 24 hours (median, 48 hours). The median time delay between MRI and PET was 68 minutes (interquartile range, 52–140). All patients had a MCA stroke (right/left hemisphere: 8/14). The median National Institutes of Health Stroke Scale score on admission was 12 (interquartile range, 6–14). ICA stenosis was present in 9 patients ipsilateral to the infarct. No patient presented with a contralateral ICA or MCA stenosis.

**ROC Curve Analysis**

The ROC curve analysis was performed separately for every patient’s regions of interest and each modality. Representative data of 1 patient are displayed in Figure 3. The mean AUC values as well as the optimal absolute and relative PF thresholds for each patient and PW modalities are shown in the Table as a pooled analysis.

**AUC Values**

AIF placement within the proximal or distal MCA segments ipsi- or contralateral to the infarct did not significantly influence the accuracy of PF detection. The AIF-dependent maps of CBF (mean AUC from all 7 AIF placements, 0.93) or Tmax (mean AUC, 0.93) performed best. However, the performance of AIF-independent TTP maps was comparable (mean AUC, 0.91).

**PF Thresholds**

The optimal absolute PF thresholds were clearly influenced by the AIF location. This AIF dependence was most pronounced for CBF and CBV and less for MTT and Tmax. However, AIF placement did not significantly influence the optimal relative PF thresholds (Table; Figure 4; Supplemental Table S1; http://stroke.ahajournals.org).

**Effect of Stenosis and Time of Imaging**

For all AIF-dependent PWI maps, there was no significant difference: (1) if the AIF was chosen from patients with or without ICA stenosis for mean AUC values (CBF 0.94 versus 0.93; CBV 0.72 versus 0.74; MTT 0.78 versus 0.76; Tmax 0.92 versus 0.93), mean absolute PF thresholds (CBF 40.12 versus 45.02; CBV 1.92 versus 1.92; MTT 3.85 versus 3.78; Tmax 5.6 versus 5.6), and mean relative PF thresholds (CBF 0.45 versus 0.49; CBV 0.48 versus 0.51; MTT 0.83 versus 0.83; Tmax 3.11 versus 3.22); and (2) for early versus late imaging for the threshold independent mean AUC values (CBF 0.93 versus 0.92; CBV 0.71 versus 0.71; MTT 0.77 versus 0.75; Tmax 0.90 versus 0.90), the mean absolute PF threshold values (CBF 45.02 versus 45.02; CBV 1.92 versus 1.92; MTT 3.85 versus 3.85; Tmax 5.6 versus 5.6), and for mean relative PF threshold values (CBF 0.49 versus 0.50; CBV 0.52 versus 0.51; MTT 1.09 versus 1.12; Tmax 3.01 versus 3.12).

**Interobserver Reliability**

The intraclass correlation coefficients of the PW-based CBF, CBV, MTT, and Tmax values from the affected hemisphere comparing AIF placement by the raters in 7 different locations were excellent (Supplemental Table S2).

**Discussion**

Three main issues have to be discussed regarding the influence of AIF placement on PW maps: (1) the threshold-
The AUC from the ROC curve analysis is a threshold-independent measure. It describes the performance of quantitative as well as relative PW maps to detect PF (<20 mL/100 g/min) regardless of absolute or relative flow values. We found that the AIF placement does not significantly influence this threshold independent performance of the PW maps to detect PF although absolute PW values increase with more distal AIF placement. One explanation might be a global increase of PW CBF values. In our patient sample, selecting the AIF from the ischemic compared with the nonischemic hemisphere did not result in a statistically significant difference of the AUC value. These findings are consistent with a previously published report in acute stroke choosing different AIF locations.13 Our results show significantly higher AUC values for CBF and Tmax for all AIF placements and make these perfusion maps well suitable for stroke studies. However, the performance of the AIF-independent relative TTP maps was comparable and makes TTP a useful measure if extended postprocessing is not feasible.14,17,19

Absolute PF Thresholds

On PWI, the AIF is crucial for quantitative perfusion measurement and thus represents an important source of variability.5 We found that the absolute PF thresholds on maps of CBF and CBV are strongly and maps of Tmax and MTT moderately influenced by the AIF placement: distal AIF placement leads to a smaller AIF amplitude, resulting in overestimation of, for example, PW CBF values.20 Additionally, underestimation of the real AIF may occur because of low temporal resolution or partial volume averaging of the artery with surrounding brain tissue in more distal vessels.21 We found significantly higher absolute PW CBF and CBV threshold values for distal AIF placement. This influence is most pronounced for maps of CBF and CBV and less for MTT and Tmax. For absolute CBF maps, we identified the best AIF placement proximal and contralateral to the infarct (ie, cM1) leading to the best delineation of PET CBF <20 mL/100 g/min. In our patient sample, comparing absolute PW maps to detect PF although absolute PW values increase with more distal AIF placement. One explanation might be a global increase of PW CBF values. In our patient sample, selecting the AIF from the ischemic compared with the nonischemic hemisphere did not result in a statistically significant difference of the AUC value. These findings are consistent with a previously published report in acute stroke choosing different AIF locations.13 Our results show significantly higher AUC values for CBF and Tmax for all AIF placements and make these perfusion maps well suitable for stroke studies. However, the performance of the AIF-independent relative TTP maps was comparable and makes TTP a useful measure if extended postprocessing is not feasible.14,17,19

Relative PF Thresholds

For relative PF thresholds, no significant influence was found according to different AIF placement. This emphasizes that relative thresholds are an input-independent and robust measure to detect the PF threshold. Therefore, relative PF thresholds might be more useful in the acute stroke setting than absolute perfusion values to detect PF because the choice of an AIF within a certain segment is not essential.

### Table. Median Equal Sensitivity and Specificity Threshold Penumbra Flow Cutoff Values of CBF, CBV, MTT, Tmax, and TTP With Their Corresponding Mean Sensitivity and Specificity and the Median AUC Results Derived From the Receiver Operating Characteristic Curve Analysis

<table>
<thead>
<tr>
<th>PWI</th>
<th>AIF</th>
<th>Absolute PF Threshold</th>
<th>Mean Sensitivity</th>
<th>Mean Specificity</th>
<th>Relative PF Threshold</th>
<th>AUC</th>
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<td>CBF</td>
<td>cICA-cM1</td>
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<td>87.0</td>
<td>0.51</td>
<td>0.93</td>
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<td></td>
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<td>86.6</td>
<td>0.54</td>
<td>0.94</td>
</tr>
<tr>
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<td>85.7</td>
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<td>0.93</td>
</tr>
<tr>
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<td>87.4</td>
<td>0.52</td>
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<td>79.9</td>
<td>0.60</td>
<td>0.73*</td>
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<tr>
<td></td>
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<td>79.7</td>
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<td>0.73*</td>
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<tr>
<td></td>
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<td>79.1</td>
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<td>0.74*</td>
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<td>74.6</td>
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<td>71.5</td>
<td>1.07</td>
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<td>85.9</td>
<td>75.2</td>
<td>1.07</td>
<td>0.80*</td>
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<td>87.6</td>
<td>2.73</td>
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</tr>
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<td>85.9</td>
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<td>86.8</td>
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<td>39.70</td>
<td>85.6</td>
<td>86.3</td>
<td>4.38</td>
<td>0.91</td>
</tr>
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</table>

CBF indicates cerebral blood flow (mL/100 g/min); CBV, cerebral blood volume (mL/100 g); MTT, mean transit time (sec); Tmax, time to maximum (sec); TTP, time to peak (sec); AUC, area under the curve; PWI, perfusion-weighted imaging; AIF, arterial input function; PF, penumbral flow; ICA, internal carotid artery; c/M1/2/3, AIF taken from the M1, M2, or M3 segment of the MCA contralateral/ipsilateral to the infarct; cICA-cM1, AIF taken from the ICA and M1 contralateral to the infarct; MCA, middle cerebral artery; N/A, not applicable.

*Significantly (P<0.05) lower AUC values (Mann-Whitney U rank-sum test).
Thus, the procedure of normalization by division (CBF, CBV, MTT) or subtraction (Tmax) may eliminate some of the dispersion and delay as well as some of the partial volume that affected the AIF. However, relative maps cannot be used if absolute values of CBF and CBV are required (eg, to measure an increase of collateral or global flow).

**Vessel Stenosis**

Stenosis of the ICA or MCA will theoretically result in an altered delay and dispersion of the contrast agent and may lead to errors in the AIF. The relative PF thresholds were not significantly different for the patients with and without ipsilateral ICA stenosis. One possible explanation might be that delay and dispersion were partly eliminated by the normalization procedure. In our sample size, absolute PF threshold values were not significantly different for AIFs chosen from patients with and without stenosis of the affected hemisphere, although there was a trend for lower CBF PF thresholds in patients with ipsilateral stenosis. These results are in line with a previous comparative PET study of patients with chronic carotid occlusive disease.\(^1^2\) One reason might be that we placed the AIF within the MCA where collateral supply through the circle of Willis will have joined the MCA. Therefore, the error of asymmetrical delay and dispersion introduced by proximal vessel stenosis is attenuated.\(^1^1\) It is important to mention that we avoided the stenosis for AIF placement because distortion, dispersion, and delay would lead to significant errors in the calculated PWI values.\(^4\) No patient presented with a contralateral ICA or MCA stenosis and therefore we did not have any problems choosing an AIF from this location.

**Previous Studies**

Only few acute stroke studies, using MRI exclusively, have investigated the influence of AIF placement on (1) the calculated PW maps; and (2) the morphology of the AIF. One

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Figure 4. Influence of AIF placement on PWI values in a pooled analysis. Box plots show the AIF dependence of the PW maps: (A) for “absolute” PF thresholds; (B) for “relative” PF thresholds; and (C) for AUC as a threshold-independent measure. Note that AUC and “relative” PF thresholds are not statistically dependent from the AIF location (cM1, cM2, cM3, iM1, iM2, iM3 or cICA-cM1), whereas the absolute PF threshold increases significantly for CBF and CBV with more distal AIFs. AIF indicates arterial input function; PWI, perfusion-weighted imaging; AUC, area under the curve; PF, penumbral flow; CBF, cerebral blood flow; CBV, cerebral blood volume.
study (12 patients) found the AIF from peri-infarct arteries to produce the best PW maps in terms of sensitivity and specificity to detect late infarct delineation. However, no threshold was used when defining the abnormality on PWI overestimating the tissue at risk. Another study (13 patients) found the largest PW lesion size with a threshold of Tmax delay ≥2 seconds for the AIF measured from the MCA contralateral to the infarct. This threshold however seems too low and much of the lesion volume will include oligemia. Both studies compared early PW imaging with stroke evolution on follow-up MRI and are thus hampered by secondary flow changes that might confound the results. A recent study of 132 patients with suspected ischemia found the contralateral distal segments, rather than the contralateral proximal segments, of the MCA to be the most appropriate location for AIF definition by a description of the resulting AIF morphology. However, the quality of the AIF signal itself is not necessarily a surrogate measure for PF detection on deconvolved PW maps. The reported studies did not compare the results with a gold standard for in vivo blood flow or the influence of the AIF location on the resulting PF thresholds. In this respect, our study presents the first PET-validated approach to quantify the influence of AIF placement on quantitative PF detection by MRI.

Limitations and Methodical Issues
Several limitations and methodical issues have to be discussed. Our imaging and postprocessing protocol influenced the calculation of absolute and relative PF thresholds, as discussed in part previously. First, our postprocessing tool is based on the algorithm described by Ostergaard and uses the standard singular value decomposition (SVD) commonly used in the literature. Standard singular value decomposition is provided by most MR scanner-related software packages and seems to be more sensitive to tracer delay than the circular singular value decomposition. However, both methods yield comparable results for CBF in the ischemic range according to a recent study comparing PWI and PET in acute stroke. Second, our thresholds are based on a PET-CBF threshold <20 mL/100 g/min, which is the commonly accepted PF threshold in the literature for gray matter. Therefore, our PF thresholds apply to gray matter and the thresholds for white matter may be different. Third, in our study, the best cutoff threshold for PF using the ROC curve analysis was determined by the equal sensitivity and specificity threshold, which was selected because it weights false-positive and false-negative errors equally. Depending on the individual clinical setting, a higher sensitivity or specificity might be required and therefore the threshold values might be slightly different. Fourth, the manual selection of the AIF in patients with major vessel pathologies might be associated with large observer-dependent bias. However, we found this effect not to be relevant and our results are in line with previous studies testing for interobserver variability. Fifth, our sample size was limited but presents the largest PET-MR patient sample in acute stroke. Sixth, the quantitative PF thresholds do not necessarily represent absolute or real quantitative thresholds. Discrepancies exist between MR-based and absolute PET or Xenon-CT based perfusion measurements. The individual variability of the perfusion values may have been caused by the different PWI sequence parameters as well as by partial volume effects and dispersion on the AIF. To increase quantitiveness, we provided in a previous study an individual calibration procedure for PW images (derived from cICA and cM1 AIFs) based on quantitative 15O-water PET. This easy-to-use MR-based and PET-validated calibration improved the detection of PF in the acute stroke setting.

Conclusions
Using quantitative PET as a reference method, we have shown that there is a significant influence of the AIF location on quantitative PW maps. The optimal input-dependent PW maps for PF threshold detection are CBF and Tmax. If using absolute PF thresholds, the AIF is crucial for the detection of PF because quantitative PF thresholds increase with more distal AIF placement. Therefore, to yield quantitative results, using a CBF threshold of 20 mL/100 g/min or a Tmax threshold of 6 seconds, PW maps should be processed by AIFs chosen from a proximal (eg, cM1) branch contralateral to the affected hemisphere. If choosing relative PF thresholds, however, the location of AIF placement is not relevant for the detection of the optimal PF threshold. This emphasizes the usefulness of relative PF thresholds in the clinical setting where time is crucial. Moreover, our data support the AIF-independent measure TTP as a simple and robust alternative measure if detailed postprocessing is not feasible. Awareness of these results is important not only for the standardization of AIF placement, but also for proper use of PW maps.

Acknowledgments
We thank Dr U. Malzahn (Center for Stroke Research Berlin, Charite Berlin) for statistical advice and Dr H.-J. Wittsack (Department of Radiology, University of Dusseldorf) for providing the Stroke-Tool software.

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Disclosures
None.

References


## ONLINE SUPPLEMENT

### SUPPLEMENTAL TABLES

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**Supplementary Table S1:** Variation of median AUC values. AUC 25%/75%, Absolute PF threshold 25%/75% and Relative PF threshold 25%/75%, indicate interquartile range (IQR) of median AUC, Absolute and Relative PF thresholds values; c/iM1/2/3, indicates AIF taken from the M1, M2 or M3 segment of the MCA contralateral/ipsilateral to the infarct; cICA-cM1, AIF taken from the ICA and M1 contralateral to the infarct; PW, perfusion weighted.
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**Supplementary Table S2:** Intraclass correlation coefficients (ICC) of the PW based CBF, CBV, MTT and Tmax values from the affected hemisphere comparing AIF placement by the two raters in 7 different locations. c/iM1/2/3, indicates AIF taken from the M1, M2 or M3 segment of the MCA contralateral/ipsilateral to the infarct; cICA-cM1, AIF taken from the ICA and M1 contralateral to the infarct; PW, perfusion weighted.
Influence of the Arterial Input Function on Absolute and Relative Perfusion-Weighted Imaging Penumbral Flow Detection: A Validation With 15O-Water Positron Emission Tomography

Olivier Zaro-Weber, Walter Moeller-Hartmann, Wolf-Dieter Heiss and Jan Sobesky

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