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Quantitative Assessment of Core/Penumbra Mismatch in Acute Stroke

CT and MR Perfusion Imaging Are Strongly Correlated When Sufficient Brain Volume Is Imaged

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Background and Purpose—Our purpose was to determine (1) the correlation between quantitative CT and MR measurements of infarct core, penumbra, and mismatch; and (2) whether the difference between these measurements would alter patient selection for stroke clinical trials.

Methods—We studied 45 patients with acute middle cerebral artery stroke imaged a mean of 3.8 hours after onset (range, 0.48 to 8.35 hours) who underwent CT perfusion and MR diffusion (DWI)/perfusion imaging within 3 hours of each other. The DWI and MR-mean transit time (MTT) abnormalities were visually segmented using a semiautomated commercial analysis program. The CT-cerebral blood volume) and CT-MTT lesions were automatically segmented using a relative cerebral blood volume threshold of 0.56 and a relative MTT threshold of 1.50 on commercially available software. Percent mismatch was defined as [(MTT−DWI)/DWI volume]×100. Pearson correlation coefficients were calculated.

Results—There were significant correlations for DWI versus CT-cerebral blood volume lesion volumes (r^2=0.88, P<0.001), for MR-MTT versus CT-MTT lesion volumes(r^2=0.86, P<0.001), and for MR-MTT/DWI versus CT-MTT/CT-cerebral blood volume mismatch lesion volumes(r^2=0.81, P<0.001). MR perfusion and CT perfusion agreed for determining: (1) infarct core < versus ≥100 mL in 41 of 45 (91.1%); (2) MTT lesion size < versus >2 cm diameter in 42 of 45 (93.3%); (3) mismatch < versus >20% in 41 of 45 (91.1%); and (4) inclusion versus exclusion from trial enrollment in 38 of 45 (84.4%) patients. Six of 7 disagreements were due to inadequate CT coverage.

Conclusion—Advanced MR and CT perfusion imaging measurements of core/penumbra mismatch for patient selection in stroke trials are highly correlated when CT perfusion coverage is sufficient to include most of the ischemic region. Although MR is currently the preferred imaging method for determining core and penumbra, CT perfusion is comparable and potentially more available. **(*Stroke*. 2008;39:2986-2992.)**

Key Words: acute ischemic ■ acute stroke ■ CT ■ MRI ■ penumbra ■ perfusion CT imaging ■ perfusion MR imaging

The only US Food and Drug Administration-approved medical therapy for acute stroke to date is intravenous tissue plasminogen activator administered within 3 hours of symptom onset. However, there is increasing evidence that identification of potentially salvageable brain tissue with advanced MR and CT imaging may allow the selection of patients who can be effectively and safely treated with intravenous thrombolysis for up to 9 hours postictus.[1–5] Specifically, the mismatch between infarct core (brain likely to be irreversibly infarcted regardless of treatment) and ischemic penumbra (hypoperfused brain at risk for infarction in the absence of reperfusion) may identify patients with both a low hemorrhagic risk (small core) and a high likelihood of treatment benefit (large penumbra).

In clinical practice, the core can be operationally defined using either MR diffusion-weighted imaging (DWI) or CT cerebral blood volume imaging (CT-CBV), and penumbra with either MR or CT perfusion-weighted imaging (MRP or CTP). However, the major completed clinical trials supporting the use of intravenous thrombolysis beyond 3 hours (Desmoteplase in Acute Ischemic Stroke [DIAS], Dose Escalation of Desmoteplase for Acute Ischemic Stroke [DEDAS], and Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution [DEFUSE]) and trials still in

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Table 1. Patient Demographics

	Mean*	Range
Age	72.7	24–97
NIHSS*	13.0	2–27
Time to first image	3:39	0:29–8:21
Time CTP to MRI	0:42	0:08–2:08
Sex	21 male	24 female
Side	22 left	21 right

*NIHSS is expressed as median rather than mean because it is not a normal distribution.

progress (Echoplanar Imaging Thrombolysis Evaluation Trial [EPITHET], ReoPro Retavase Reperfusion of Stroke Safety Study Imaging Evaluation [ROSIE], and MR and Recanalization of Stroke Clots Using Embolectomy [MR RESCUE]) have all used DWI/MRP mismatch for patient selection.[1–3,6]

CT scanners are much more widely available and accessible in emergency rooms than are MRI scanners and imaging patients with acute stroke as rapidly as possible is of paramount importance. Therefore, we sought to determine if CTP can be used in place of MRP for patient selection in clinical trials. Specifically, 3 inclusion criteria for major clinical trials aimed at extending the time window for intravenous thrombolysis beyond 3 hours are: (1) mean transit time (MTT) lesion diameter <2 cm; (2) core lesion size <one third of the middle cerebral artery (MCA) territory (approximately 100 mL); and (3) core/penumbra mismatch >20%. We therefore sought to determine: (1) the correlation between quantitative CT and MR measurement of mismatch; and (2) whether the difference between these measurements, using current clinical protocols, would alter patient selection for stroke clinical trials.

Methods

Patient Selection

This retrospective study was approved by our Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act. Review of our radiology database from June 2004 to August 2006 identified 47 consecutive patients with acute MCA and/or anterior cerebral artery stroke who had: (1) CTP within 9 hours of symptom onset; (2) MR diffusion and perfusion imaging within 3 hours subsequent to CTP; (3) unilateral stroke; (4) no evidence of old infarction; and (5) technically adequate images from both CTP and MRP. For our patients with acute stroke, we routinely obtain CTP and MRP. Initially, the patient receives a noncontrast CT and CT angiography to determine whether the patient is a candidate for recanalization therapy. We obtain a CTP because with only a few extra minutes of scanning and automated software, we can obtain quantitative core penumbra mismatch data very rapidly. We then transfer the patient to the MR scanner and obtain DWI and MRP because MRP has better coverage (whole brain) than CTP and unlike CTP has been widely accepted in clinical trials.

Two of these cases were subsequently excluded after review of the imaging due to reperfusion between the CTP and MRP acquisitions. Ultimately, 45 patients were included; their demographic and clinical characteristics are shown in Table 1. Thirty-four patients had proximal vascular occlusions (internal carotid artery, M1 or M2), 2 had distal anterior cerebral artery occlusions, one had a distal MCA occlusion, and 8 had no visible occlusion on CT and/or MR angiogram. The National Institutes of Health Stroke Scale (NIHSS) score was performed by the admitting neurologist. In 4 patients, an admission NIHSS was not recorded and was recalculated from the well-documented admission neurological examination.[7] For one additional patient, an NIHSS score was not recorded and the admission note was insufficiently detailed to recalculate one. No patients were treated with intra-arterial recanalization procedures before CT or MR perfusion imaging. Six patients underwent intra-arterial recanalization after both studies. Twenty patients received intravenous tissue plasminogen activator, 9 before imaging, 4 between CTP and MRP, and 7 after both studies.

MRI Image Acquisition

MR imaging was performed on a 1.5-Tesla Signa whole-body scanner (GE Medical Systems, Milwaukee, Wis) with echo planar capabilities.

DWI images were obtained using single-shot, spin echo echoplanar imaging with sampling of the entire diffusion tensor. Six high b-value images corresponding to diffusion measurements in different gradient directions were acquired in addition to a single low b-value image. Double inversion pulses were used to help reduce eddy current effects. The high b value was 1000 s/mm^2 and the low b value was 0 s/mm^2. A TR of 5000 ms was used. The TE for each scan was the minimum possible, typically between 90 and 100 ms. Other parameters are field of view of 22×22 cm, image matrix of 128×128 pixels, slice thickness of 5 mm with 1-mm gap, and 5 signal averages. As many axial slices as were needed to cover the entire brain were included, typically 22 to 25. Isotropic DWI images and apparent diffusion coefficient maps were reviewed.

Perfusion-weighted imaging was performed using a dynamic susceptibility contrast technique. Serial echoplanar gradient echo images were acquired with TR/TE of 1500/40 ms, field of view 22 cm, matrix 128×128, and slice thickness 5 mm with a 1-mm interslice gap. A complete volume of 16 slices was acquired every 1.5 seconds and 46 such volumes were acquired so that the total imaging time required by the sequence was 1 minute 9 seconds. Ten seconds after the beginning of image acquisition, 20 mL of gadopentetate dimeglumine 0.5 mmol/mL was administered through a peripheral intravenous catheter at a rate of 5 mL/s. This was followed immediately by the administration of 20 mL of normal saline at the same rate.

MRI Image Processing

Dynamic susceptibility contrast images were used to generate signal intensity-versus-time curves for each pixel in the imaged volume. These curves were integrated to yield maps of CBV for each pixel. Cerebral blood flow was calculated for each pixel by deconvolution using the singular value decomposition technique.[8,9] A global arterial input function was derived from the MCA ipsilateral to each patient's infarct. Vascular MTT was calculated by dividing CBV by cerebral blood flow.

Postprocessing Image Analysis of MRI

Visually detected DWI and MTT abnormalities were manually segmented by a research assistant using a semiautomated commercial analysis program (Analyze 7.0; AnalyzeDirect). Final outlines were manually edited by a single experienced neuroradiologist. For each patient, volumes and percent mismatches were calculated using all DWI and MTT slices and using only those slices that covered regions that were also covered with CTP. Percent mismatch was defined as [(MTT−DWI)/DWI]×100%. Cases were classified according to DWI lesion size (greater or less than 100 mL), mismatch (greater or less than 20%), and MTT lesion volume (greater or less than 4.19 mL−the volume of a sphere with a diameter of 2 cm).

CT Perfusion Image Acquisition

CTP imaging was performed on a multidetector helical scanner (16- or 64-slice LightSpeed; GE Healthcare). Image acquisition was performed as a cine series (45 to 70 seconds at one image[s]) beginning 5 seconds after power injection (through a peripheral intravenous catheter, 18 to 20 gauge) of 35 to 40 mL of contrast

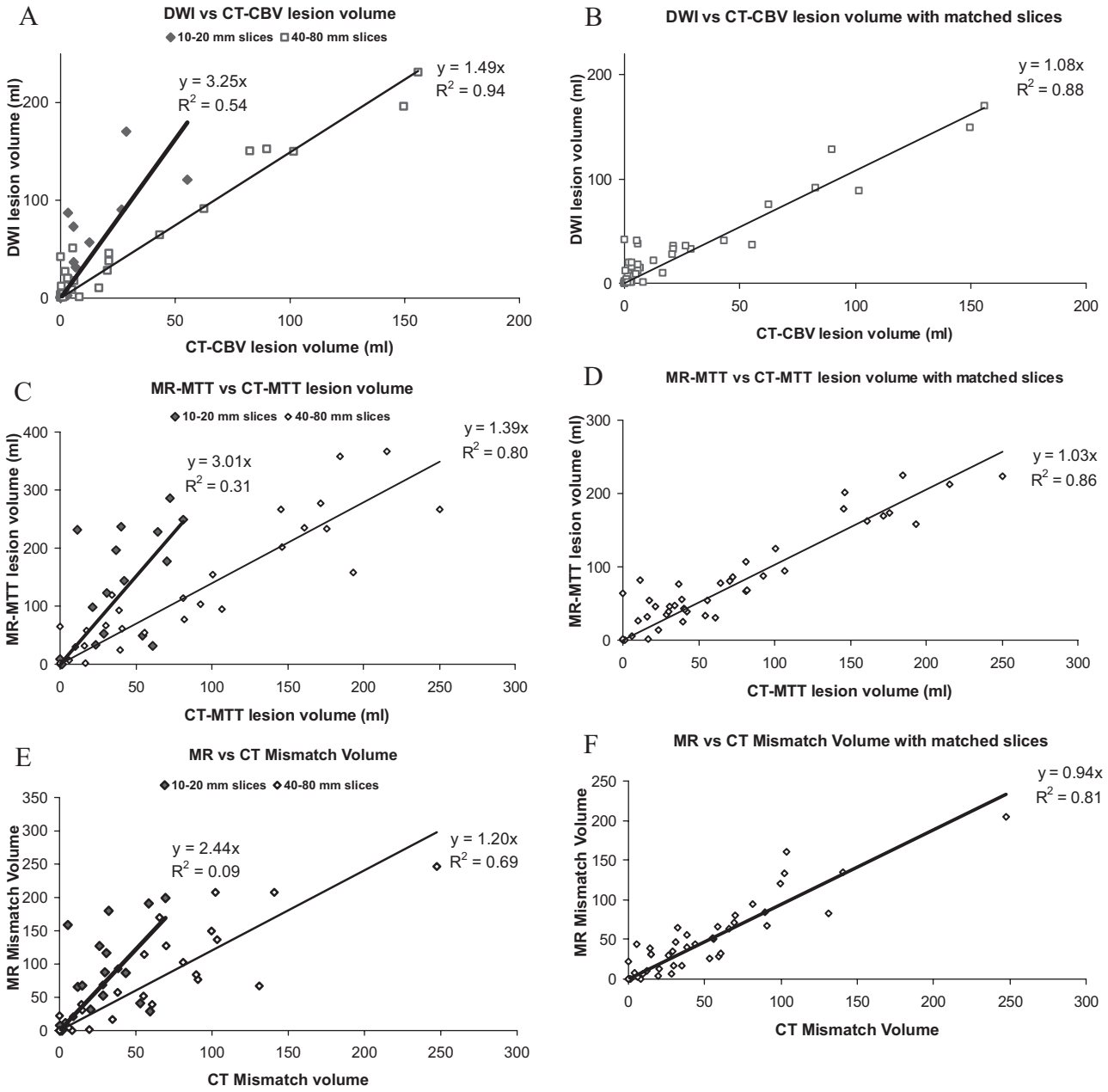

Figure 1. A–F, Graphs of correlations between MRP and CTP core, penumbra, and mismatch volumes. Correlations of CT-CBV versus MR-DWI lesion volumes in 10 to 20 mm (R^2=0.54, slope=3.25) and 40 to 80 mm (R^2=0.94, slope=1.49) thick CTP slices. B, Correlation of CT-CBV versus MR-DWI lesion volumes in matched (R^2=0.88, slope=1.08) slices. C, Correlation of CT-MTT versus MR-MTT in 10 to 20 (R^2=0.31, slope=3.0) and 40 to 80 mm (R^2=0.80, slope=1.39) thick CTP slices. D, Correlation of CT-MTT versus MR-MTT in matched slices (R^2=0.86, slope=1.03). E, Correlations of MR (MTT−DWI) versus CT (MTT−CBV) mismatch volumes in 10 to 20 (R^2=0.09, slope=2.44) and 40 to 80 mm (R^2=0.69, slope=1.20) thick CTP slices. F, Correlations of MR (MTT−DWI) versus CT (MTT−CBV) mismatch volumes in matched slices (R^2=0.81, slope=0.94). All correlation coefficients significantly improve with increasing slab thickness (P<0.05 for Group 2 versus Group 1). The higher correlation coefficient values for the CT-MTT versus MR-MTT lesion volumes and the CT versus MR mismatch volumes when the MRI volumes were calculated using only those slices that corresponded to the imaged CTP slabs, however, are not significantly different from the corresponding values in Group 2 (P>0.05). R^2=Pearson correlation coefficient; y=slope. 10 to 20 mm=Group 1, 40 to 80 mm=Group 2.

(Isovue 370; Bracco Diagnostics, Princeton, NJ) at 5 to 7 mL/s with a normal saline "chaser" bolus. Imaging parameters were 80 kVp, 200 mA, 1-second rotation time. Coverage consisted of slabs positioned parallel and superior to the orbital roof (to avoid radiation to the lens). On the 16-slice scanner, each slab consisted of one or 2 slices of 10-mm thickness or 4 slices of 5-mm thickness. On the 64-slice scanner, each bolus administration of contrast resulted in a 40-mm slab consisting of 8 slices of 5-mm thickness. Four patients received 2 such contrast bolus injections resulting in 2 40-mm slabs for a total of 80-mm coverage.

CT Perfusion Image Processing and Analysis

For CTP analysis, CBV and MTT maps were created from CTP data with commercially available semiautomated perfusion analysis software (Philips Brain Perfusion 2004; Philips Medical System). The arterial input region of interest was selected from the MCA con-

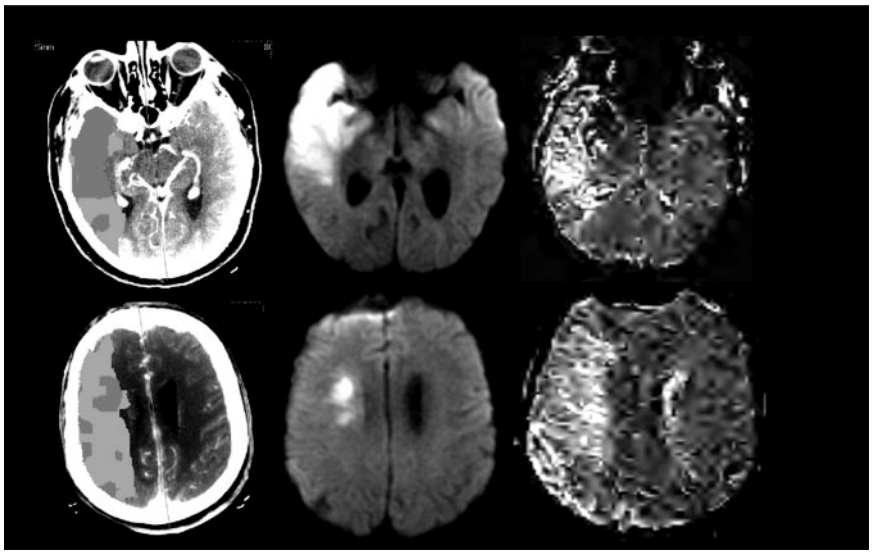

Figure 2. MRP and CTP images. Good correlation between CTP and MRP lesion volumes and mismatch measurement. A 67-year-old man with NIHSS 18 and acute right MCA stroke; CTP performed 3:46 after symptom onset with 40 mm of coverage (CT-CBV [dark gray], 43.2 mL; CT-MTT (light gray), 146.51 mL; mismatch volume, 103.31 mL; mismatch percent=239.1), MRP performed 0:38 after CTP (DWI, 64.6 mL; MR-MTT, 201.0 mL; mismatch volume, 136.4 mL; mismatch percent, 196.0).

tralateral to the infarct. The venous input region of interest was selected from the superior sagittal sinus. Infarct core was segmented based on a CBV threshold of 56% relative to the opposite side. The threshold chosen was based on the results of a pilot study, which compared DWI and CBV lesion volumes using thresholds of 46%, 56%, and 66% of the contralateral normal side as well as a 2 mL/100-g absolute threshold; the DWI CBV correlation was optimal using the 56% threshold.[10] Ischemic penumbra was segmented based on a MTT threshold of 150% relative to the contralateral side; this threshold was chosen based on a prior published report.[11] Using these thresholds, the software calculated the areas of the CBV and MTT lesions for each slice. These areas were multiplied by the slice thickness (5 mm or 10 mm) to determine the CBV and MTT lesion volumes. For patients with 2 CTP slabs, CBV and MTT volumes were calculated for each slab and summed for a total volume. Total CTP slab thickness was recorded as follows: 3 patients had 10 mm, 14 patients 20 mm, 24 patients 40 mm, and 4 patients 80 mm thickness. Percent volume mismatch was defined as [(MTT−CBV)/CBV]×100%. Cases were classified according to CBV lesion size (greater or less than 100 mL), CBV/MTT mismatch (greater or less than 20%), and MTT lesion volume (greater or less than 4.19 mL).

Statistical Analysis

Pearson correlations were used to compare CTP CBV versus MRI DWI lesion size, CTP MTT versus MRI MTT lesion size, and CT mismatch volume versus MR mismatch volume. Fisher's z transformation was used to determine whether Pearson correlation coefficients were statistically significantly different. Kappa statistics were calculated for agreement between CTP and MRP clinical trial selection criteria.

Results

Patient demographics are shown in Table 1. Mean DWI lesion volume was 48.6 mL (0 to 247 mL) and mean CT-CBV lesion volume was 23.0 mL (0 to 156 mL; r^2=0.74; P<0.001). Mean MR-MTT lesion volume was 141.5 mL (0.4 to 388 mL), and mean CT-MTT lesion volume was 78 mL (0.2 to 306 mL; r^2=0.45; P<0.001). Mean MR-MTT/DWI difference was 81.55 mL (0.01 to 246.4) and mean CT-MTT/CBV difference was 47.65 mL (0.07 to 247.4; r^2=0.34; P<0.001). The patients were divided into 2 groups according to the thickness of the CTP slab; Group 1 included 17 patients with 10- or 20-mm thickness and Group 2 included 28 patients with 40- or 80-mm thickness.

For Group 1, there were statistically significant correlations between MR-DWI and CT-CBV lesion volumes (r^2=0.54, P<0.001) and between CT-MTT and MR-MTT lesion volumes (r^2=0.31, P<0.001), but not between CT and MR mismatch volumes. For Group 2, there were statistically significant correlations among all 3 comparison pairs, and all 3 correlation coefficients were significantly higher than the corresponding values for Group 1 with r^2=0.94 (P<0.001) for DWI versus CT-CBV, r^2=0.80 (P<0.001) for CT-MTT versus MR-MTT and r^2=0.69 (P<0.001) for CT-MTT/CBV mismatch volume versus MR-MTT/DWI mismatch volume. The correlation coefficients for CT versus MR-MTT (r^2=0.86, P<0.001) and CT versus MR mismatch volume (r^2=0.81, P<0.001) further improved when MRI volumes were calculated using only those slices that corresponded to the imaged CTP slabs, although they were not significantly different (P>0.05) from the corresponding values in Group 2 (Figures 1 and 2; Table 2).

Patient selection with CTP versus MRP maps, using 3 different clinical trial inclusion and exclusion criteria, is summarized in Table 3. For determination of infarct core greater versus less than 100 mL, the CT-CBV lesion volume agreed with the MR-DWI lesion volume in 91% of cases (kappa=0.56). All 4 cases of disagreement (one with 10 mm, one with 20 mm, and 2 with 40-mm coverage) resulted from the CTP slab not covering the entire lesion. For determination of MTT lesion volume greater versus less than 4.19 mL, CT-MTT lesion volume agreed with MR-MTT lesion volume in 93% of cases (kappa=0.63). For the 2 cases (one with 20-mm and one with 40-mm CTP coverage) in which the CT-MTT lesion volume was less than and the MR-MTT volume was greater than 4.19 mL, the CTP slab placement did not cover the lesion. For the one case (with 40-mm coverage) in which the CT-MTT lesion volume was greater than and the MR-MTT lesion volume was less than 4.19 mL, the automated CTP software segmentation was incorrect (Supplemental Figure I, available online at http://stroke.ahajournals.org). For determination of whether mismatch was greater or less than 20%, the CT mismatch agreed

Table 2. Correlation of Advanced CT versus MR Lesion Volume Values

	All Patients		10 to 20 mm (Group 1)		40 to 80 mm (Group 2)		Same Coverage for CTP and MRP (matched slices)	
	r^2	*P* Value	r^2	*P* Value	r^2	*P* Value	r^2	*P* Value
CT-CBV versus MR-DWI lesion volumes	0.74	<0.001	0.54*	<0.001	0.94**	<0.001	0.88***	<0.001
CT-MTT versus MR-MTT lesion volumes	0.45	<0.001	0.31†	<0.001	0.80††	<0.001	0.86†††	<0.001
CT-MTT minus CBV versus MR-MTT minus DWI lesion volumes	0.34	<0.001	0.09‡	>0.05	0.69‡‡	<0.001	0.81‡‡‡	<0.001

For CT-CBV versus MR-DWI, the difference in r^2 between ** and *** is not significant at $P=0.08$. The difference between * and ** is significant at $P<0.001$ as well as between * and *** at <0.01.

For CT versus MR-MTT, the difference in r^2 between †† and ††† is not significant at $P=0.18$. The difference between † and †† is significant at $P<0.01$ as well as between † and ††† at <0.001.

For mismatch volumes, the difference in r^2 between ‡‡ and ‡‡‡ is not significant at $P=0.13$. The difference between ‡ and ‡‡ is significant at $P<0.01$ as well as between ‡ and ‡‡‡ at <0.001.

with MR mismatch in 91% of cases (kappa=0.31). In 4 cases, the MRP mismatch was less than 20% and the CTP mismatch was greater than 20%. In 3 of these cases (2 with 20-mm and one with 40-mm coverage), the MTT lesion size was very small (<4.19 mL), making percentage mismatch less reliable, whereas the fourth case (with 40-mm coverage) had the incorrect CTP segmentation previously described.

Finally, we combined these criteria to determine the agreement between CTP and MRP for patient selection in clinical trial enrollment (Tables 3 and 4). For MR versus CT "core" volume less than 100 mL, "penumbra" volume >4.19 mL and mismatch >20%, we found an 84% agreement (kappa=0.54; Figure 1). Two patients (one with 20-mm and one with 40-mm CTP coverage) met selection criteria for clinical trial enrollment based on MRP but not CTP findings, because the CTP slab did not fully cover the ischemic lesion and so the CT-MTT volume was inaccurately determined to be less than 4.19 mL. Four patients (one with 10-mm, one with 20-mm, and 2 with 40-mm CTP coverage) met selection criteria for clinical trial enrollment based on CTP but not MRP findings, again due to inadequate CTP coverage, with underestimation of the CT-CBV volume at <100 mL. One patient (with 40-mm CTP coverage) met selection criteria for clinical trial enrollment based on CT but not MR findings, because the CTP segmentation overestimated MTT lesion size and mismatch. When we excluded cases of disagreement attributable to inadequate CTP coverage, overall agreement for patient selection in a clinical trial increased to 97.8% (kappa=0.091).

Discussion

Advanced MR and CTP imaging measurements of core/penumbra mismatch for patient selection in stroke clinical trials are strongly correlated when CTP coverage is sufficient to include most of the ischemic region using currently standard scanning protocols. Specifically, when using the combined criteria of ischemic core lesion (CT-CBV or MR-DWI) <100 mL, penumbra-core (CT-MTT/CBV and MR-MTT/DWI) mismatch of >20%, and penumbra (CT-MTT or MR-MTT) >2 cm diameter, we found an overall 84% agreement between CTP and MRP for enrollment selection. In addition, we found a greater than 90% agreement between CTP and MRP when each criterion was considered individually. Moreover, the majority of cases of disagreement could be attributed to inadequate CT coverage. When we exclude cases of disagreement due to inadequate CT coverage, overall agreement for patient selection increased to 97.8% (kappa=0.091).

These results validate the use of advanced CT imaging for the selection of patients for acute stroke clinical trials. One reason that these results are important is that the success of an acute stroke clinical trial depends on assessing core and penumbra mismatch lesion size in a rapid and reproducible manner across multiple centers. We have demonstrated that commercially available CTP software allows clinically feasible, rapid automatic segmentation and volumetric measurement of CBV lesion size, MTT lesion size, and mismatch lesion size that correlates well with semiautomated volumet-

Table 3. Comparison of Clinical Trial Patient Selection Criteria Agreement for CTP versus MRP*

Inclusion Criterion	MRP and CTP Both Agreed	MR and CTP Both Disagreed	MR Disagreed	CT Disagreed	Percent Agreement
<100 mL DWI/CT-CBV	38	3	4	0	91.1
>4.19 mL MTT	39	3	1	2	93.3
>20% Mismatch	40	1	4	0	91.1
	Both Include	Both Exclude	MRP Exclude	CTP Exclude	Percent Agreement
Clinical trial inclusion	32	6	5	2	84.4

*Agreed: measurement satisfied inclusion criterion: core (MR-DWI, CT-CBV) <100 mL, penumbra (MR-MTT, CT-MTT) >4.19 mL, and mismatch (MR-MTT/DWI, CT-MTT/CBV >20%. Disagreed: measurement did not satisfy inclusion criterion: core (MR-DWI, CT-CBV) >100 mL, penumbra (MR-MTT, CT-MTT) <4.19 mL, and mismatch (MR-MTT/DWI, CT-MTT/CBV) <20%. Include: MRP or CTP satisfied all three criteria. Exclude: MRP or CTP did not meet at least one criterion.

Table 4. Patients in Whom There Was a Discrepancy Between CTP and MRP for Clinical Trial Selection Criteria

	CT-CBV, mL	MR-DWI, mL	CT-MTT, mL	MR-MTT, mL	CT Mismatch, %	MR Mismatch, %	CTP Slab Thickness, mm
Patient 1*	89.9	152.7	245.5	267.0	61.8	74.8	40
Patient 2	82.5	150.5	184.8	358.0	123.9	137.9	40
Patient 3	28.6	170.4	40.6	263.0	41.7	38.5	10
Patient 4	55.2	121.2	81.5	248.3	47.5	104.8	20
Patient 5†	0.03	42.1	0.09	64.4	255.8	53.0	40
Patient 6	0.0	1.8	0.28	9.4	NC	422.2	20
Patient 7‡	8.1	1.1	16.5	1.2	103.7	9.1	40

*For patients 1 to 4, the CTP measurement of infarct core (CT-CBV) was less than, whereas the MR measurement of core (DWI) was >100 mL.

†For patients 5 and 6, the CT measurement of penumbra (CT-MTT) was less than, whereas the MR measurement of penumbra (MR-MTT) was >4.19 mL.

‡For patient 7, the MR measurement of penumbra (MR-MTT) was less than, whereas the CT measurement of penumbra (CT-MTT) was >4.19 mL; and the MR measurement of mismatch (MTT-DWI) was less than, whereas the CT measurement of mismatch (MTT-CBV) was >20% percent. The CT segmented lesions were in different locations than those segmented on MRI.

NC indicates not calculable because the denominator is 0.

ric measurement of DWI lesion size, MR-MTT lesion size, and MR percent mismatch lesion size. Such software is currently commercially available from multiple vendors, including both Philips and GE Healthcare. Because semiautomated segmentation methods for calculating DWI and MTT are relatively time-consuming and impractical in the acute stroke setting, and there are no commercially available automatic segmentation tools for MRP, the selection criteria for most MR-based clinical trials have been based on subjective visual assessment of DWI lesion volume being less than one third of the MCA territory (or less than approximately 100 mL) and the DWI/transit time mismatch being greater than 20%. Compared with quantitative analyses, these subjective visual assessments have the potential to have poorer reliability.

Our results are also noteworthy for other reasons. Imaging patients with acute stroke as rapidly as possible is of paramount importance. In general, CT scanners are more widely available and accessible in emergency rooms than are MRI scanners, and acute stroke CT (noncontrast CT, CT angiography, and CTP) scan time is generally less than that of acute stroke MR (DWI, MR angiography, and MRP) scan time. Furthermore, patients undergoing CT scanning do not require extensive screening to assure that they do not have metal in or on their bodies, and they do not require specialized (MR-compatible, nonferromagnetic) monitoring equipment. In addition, CT scanning costs less than MR scanning.

We are aware of only one other study that compared CTP and MRP in selecting stroke patients for acute treatment.[12] In that study, the authors found 97.6% agreement between CTP and MRP for patient selection. The higher agreement between the 2 modalities in that study can be explained in part by the fact that CTP coverage was 4 cm in all cases, whereas some of our cases had only 1 or 2 cm of coverage. Indeed, in our study, when we exclude cases of disagreement due to inadequate CT coverage, overall agreement for patient selection increased to 97.8%. It is also noteworthy that their comparison was based on visual assessment, whereas ours was based on quantitative assessment.

The major drawback of CTP for acute stroke imaging is limited coverage. Indeed, most of the discrepancies between CTP and MRP in our study could be attributed to the CTP slab not covering the entire lesion. This limitation will be minimized going forward as more centers purchase 64-slice scanners, which allow 4 cm of coverage per slab. However, there was disagreement between CTP and MRP for patient selection in 4 of our subjects, even with 40-mm coverage. Therefore, one should consider using 2 contrast boluses or "shuttle mode" scanning technique, both of which can double coverage.[13] When selecting the slab to be covered in a CTP acquisition, careful consideration of the clinical data, noncontrast CT, and CT angiography findings can also increase the likelihood of appropriate coverage of the ischemic lesion.

The limitations of our study are as follows. Because CTP and MRP were performed up to 2 hours 8 minutes apart and stroke is a dynamic process, it is possible that in some patients, lesion core and ischemic penumbra volume changed between the CTP and MRP acquisitions. We excluded 2 clear cases of this phenomenon before enrollment but cannot be certain that more subtle cases were missed. Furthermore, we chose thresholds for CT-CBV and CT-MTT based on limited prior studies; it is possible that different thresholds are more appropriate and would provide a stronger correlation between CTP and MRP. In addition, we segmented MR-DWI and MTT abnormalities based on visual assessment. It is possible that choosing MR lesion volumes based on DWI and/or MTT thresholds could also improve the correlation between CT and MRI. We also chose clinical trial patient selection criteria (one third of the MCA territory for core and 20% mismatch for penumbra) based on the major large trials using "mismatch" surveyed in the introduction. A one third of MCA territory cutoff seems reasonable for "core," because analysis of the ECASS 11 data determined that there was an increased risk of symptomatic intracranial hemorrhage in patients with hypoattenuation in greater than one third of the MCA territory on unenhanced CT.[14] However, it is possible that different selection criteria using different thresholds are more appropriate, especially for penumbra, and therefore would yield different results. Indeed, this has recently been suggested by a more detailed analysis of the DEFUSE data.[15] Moreover, although MTT or some measure of transit time has become the de facto "penumbral measure of choice" for major stroke trials, it remains unproven which perfusion imaging parameter provides the best differentiation between

infarct core and penumbra in different clinical settings. It is possible that another parameter such as cerebral blood flow provides better differentiation between core and penumbra by excluding patients with benign oligemia and that we would not obtain the same results had we used other parameters.[16–18] In summary, validation and standardization of both the MR and CT definitions for "core" and "penumbra" are required.

Conclusion

Although MR is currently the preferred imaging method for measuring core, penumbra, and mismatch, CTP is quantitative and often more available. Criteria for patient selection for clinical trials are highly correlated for MR and CTP imaging when CTP coverage is sufficient to include the majority of the ischemic region.

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