Too good to treat? Ischemic stroke patients with small CT perfusion lesions may not benefit from thrombolysis

Running heading: Thrombolysis in patients with small lesions

Andrew Bivard, PhD¹, Min Lou², Christopher R Levi, FRACP¹, Venkatesh Krishnamurthy, FRACP¹, Cheng Xin³, Richard I Aviv⁴, MD, Patrick McElduff, PhD¹, Longting Lin, PhD¹, Tim Kleinig, FRACP⁵, Billy O'Brien, FRACP⁶, Kenneth Butcher⁷, Zhang Jingfen⁸, Jim Jannes, FRACP⁹, Qiang Dong³, and Mark W Parsons, PhD, FRACP¹.

1. Departments of Neurology, John Hunter Hospital, University of Newcastle, Newcastle, Australia
2. Department of Neurology, the Second Affiliated Hospital of Zhejiang University, Hangzhou. China
3. Department of Neurology, Huashan Hospital, Fudan University, Shanghai, China
4. Department of Medical Imaging, University of Toronto and Sunnybrook Health Sciences Center, Toronto Canada
5. Department of Neurology, Royal Adelaide Hospital, Adelaide, Australia
6. Department of Neurology, Gosford Hospital, Gosford, Australia
7. Division of Neurology, Department of Medicine, University of Alberta, Edmonton, Canada.
8. Department of Neurology, Baotou Central Hospital, Baotou, China
9. Department of Neurology, The Queen Elizabeth Hospital, Adelaide, Australia

Corresponding author: Andrew Bivard,

Andrew.bivard@newcastle.edu.au

Address: 1/Kookaburra Circuit, New Lambton Heights NSW 2305

Phone: (02) 4042 0000

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Abstract

Introduction: Although commonly used in clinical practice, there remains much uncertainty about whether perfusion CT (CTP) should be used to select stroke patients for acute reperfusion therapy. In this study we tested the hypothesis that a small acute perfusion lesion predicts good clinical outcome regardless of thrombolysis administration. **Methods:**

We used a prospectively collected cohort of acute ischemic stroke patients being assessed for treatment with IV-alteplase, who had CTP before a treatment decision. Volumetric CTP was retrospectively analysed to identify patients with a small perfusion lesion (<15mL in volume). The primary analysis was excellent 3-month outcome in patients with a small perfusion lesion who were treated with alteplase compared to those who were not treated.

Results: Of 1526 patients, 366 had a perfusion lesion <15mL and were clinically eligible for alteplase (212 being treated and 154 not treated). Median acute National Institutes of Health Stroke Scale score was 8 in each group. Of the 366 patients with a small perfusion lesion, 227 (62%) were mRS 0-1 at day 90. Alteplase treated patients were less likely to achieve 90 day mRS 0-1 (57%) than untreated patients (69%, RR=0.83, 95% CI 0.71-0.97, p=0.022) and did not have different rates of mRS 0-2 (72% treated patients versus 77% untreated, RR 0.93, CI 0.82-1.05, p=0.23). **Conclusion:** This large observational cohort suggests that a portion of ischemic stroke patients clinically eligible for alteplase therapy with a small perfusion lesion have a good natural history and may not benefit from treatment.

Introduction:

Although there is clear evidence for benefit of alteplase administered within 4.5 hours of ischemic stroke onset in clinical trials, clinical and non-contrast CT (NCCT) assessment do not distinguish between alteplase responders and non-responders at the individual patient level^{1,2}. By individually profiling patients with advanced CT imaging, it is now possible to identify those most likely to benefit from acute reperfusion therapy (e.g. ‘target mismatch’)^{3,4}, and to identify patients where treatment may be futile due to large infarct cores⁵, or a lack of salvageable tissue.⁶ Additionally, of the recent positive endovascular therapy trials, those that included CTP-based selection criteria tended to show greater absolute benefit as they targeted patients with the most favourable imaging profiles for reperfusion.^{7,8} These mismatch selection criteria were based on evidence from previous studies^{9,10,11,12}.

It is commonly thought that patients not fulfilling mismatch criteria have relatively large perfusion lesions on CTP, associated with severe clinical deficits and relatively poor outcomes, with or without treatment. It is noteworthy that the DEFUSE 2 and SWIFT-PRIME¹³ trials mismatch criteria excluded patients with a total lesion volume of <15mL. We recently observed in a single center cohort study that a considerable proportion of patients clinically eligible for alteplase therapy did not fulfil ‘target mismatch’ criteria due to small perfusion lesion volume (<15 mL)⁶. We aimed to further investigate if patients with a small perfusion lesion benefit from thrombolytic therapy. We hypothesized that patients with a small acute perfusion lesion would not have better outcomes when treated with alteplase.

Methods:**Patients**

Clinical and imaging information from acute ischemic stroke patients presenting to hospital within 12 hours of symptom onset at seven centers in Australia, China and Canada between 2011-2013 were prospectively collected for the International Stroke Perfusion Imaging Registry (INSPIRE). These sites were approached to be involved in the registry as they routinely perform multimodal CT prior to reperfusion therapy. Imaging acquisition parameters were standardised across sites as part of the registry design. The imaging information was baseline multimodal CT (NCCT, CTP and CT angiography), and follow-up imaging at 24-48 hours post-stroke. Clinical stroke severity was assessed at the two imaging time points using the National Institutes of Health Stroke Scale (NIHSS). Eligible patients were treated with intravenous thrombolysis according to local guidelines and the clinical judgement of the treating physician. The modified Rankin scale (mRS) was assessed 90 days after stroke. Written informed consent was obtained from all participants for their information to be collected for the registry, and the INSPIRE study was approved by the local ethics committees in accordance with Australian National Health and Medical Research Council guidelines.

Clinical information included thrombolytic treatment eligibility and time since symptom onset. Other reasons for exclusion from treatment which were captured including common clinical and NCCT contraindications (e.g. mild or improving clinical deficit, major co-morbidities, poor premorbid functional status, and extensive early ischemic change as adjudged by the treating neurologist). Given the sites involved in INSPIRE routinely performed multimodal CT prior to a treatment decision, information on thrombolytic eligibility also included questions on whether CTP results were used as an exclusion for treatment as adjudged by the treating neurologist (i.e. large ischemic core, or lack of mismatch). There were no specific treatment recommendations based on CT perfusion findings provided for this study and acute CTP processing was not standardized across sites.

Multimodal CT Protocol

Acute CT imaging included brain NCCT, CTP and CTA using either 64-, 128-, or 320-detector scanners (GE Lightspeed, Siemens Definition Flash dual source, Philips Brilliance iCT, and Toshiba Aquilion One). Axial slice coverage ranged from 41mm to 160mm. CT angiography was performed after perfusion CT with acquisition from the aortic arch to vertex¹⁴. Scanner details are summarised in Supplementary Table 1.

24 hour imaging protocol

At 24-48 hours after acute imaging, all patients, regardless of treatment, underwent a stroke MRI protocol on 1.5T or 3T scanners. The MR protocol included an axial gradient-echo T2*-weighted series, diffusion-weighted imaging (DWI), MR time of flight angiography (MRA), perfusion weighted imaging (PWI) and fluid attenuated inversion recovery (FLAIR). Follow-up infarction was defined on DWI using automated signal intensity thresholds.

CTP analysis and classification of patients

For the current analyses, all perfusion imaging was retrospectively post processed on commercial software MISTar (Apollo Medical Imaging Technology, Melbourne, Australia). Acute perfusion imaging was processed using single value deconvolution with delay and dispersion correction.¹⁵ Previously validated thresholds were applied in order to measure the volume of the acute perfusion lesion (relative delay time, DT >3 seconds) and acute infarct core (relative CBF <30%).¹⁶ All acute CTA scans were assessed for occlusion severity by a central reading group with each case being read by 2 experienced readers. The scoring system used was defined as (1) normal, (2) partial occlusion with anterograde flow, or (3) complete occlusion.^{4,14} Patients were assessed as having a small lesion if they had an acute perfusion lesion (DT>3 seconds) of <15mL. Lesions <1mL were considered artefactual.

Haemorrhage on follow-up imaging was classified as either parenchymal hematoma (PH) type 1 or 2 or haemorrhagic transformation (HT) type 1 or 2 by stroke neurologists blind to treatment and other imaging information.

Statistical analysis

Statistical analysis was performed using STATA (v13.0 StataCorp Ltd, College Station, TX). The aim of this study was to analyse clinical and imaging outcomes in patients with a small perfusion lesion (<15 mL) who were treated with alteplase compared to those with a small perfusion lesion eligible for alteplase on standard clinical grounds, but who were not treated based on CTP results. Firstly, we excluded patients from the cohort with an acute perfusion lesion >15 mL or <1 mL (See flow chart, Fig 1). Then, we excluded patients who were not eligible for alteplase on standard clinical and NCCT grounds. For the remaining patients who were all clinically eligible for alteplase, clinical and imaging variables between the treated and untreated patients were compared using Kruskal-Wallis and Fisher exact tests where appropriate. Variables included acute and 24 hour NIHSS, 3 month mRS and imaging variables (including baseline perfusion lesion and follow-up infarct volume). A general linear model with a log link function was used to determine the relative risk of achieving mRS outcomes of 0-1, 0-2, and 5-6 between patients who were treated vs those who were not treated with alteplase. Next, a propensity analysis was performed to correct for potential biases in allocation to treatment with thrombolysis arising from the non-randomized nature of the study using a two-step method.¹⁷ Firstly, a propensity score, i.e. the probability of receiving treatment with thrombolysis, was generated for each patient with the individuals demographic and clinical characteristics using a general linear model. The outcome in the general linear model was treatment with thrombolysis, and the demographic and baseline characteristics included in the model to control for confounding were sex, age, centre, baseline vessel occlusion, acute NIHSS score and time to treatment. The second step was to

calculate Inverse Probability of Treatment Weights (IPTW) from the propensity scores and use them as weights for each patient in the general linear model to calculate relative risk for treatment with thrombolysis in patients with a small acute perfusion lesion. Weighting in this way forces the model use a different amount of information from each participant to effectively 'balance' the potential confounders due to the non-randomised nature of this studies data between the two groups.

Results:

The INSPIRE database comprised 1562 patients, of whom 521 had an acute perfusion lesion of <15mL. Of these 521 patients, 102 did not meet alteplase treatment eligibility due to time of arrival (beyond 4.5 hours or uncertain onset), rapid clinical improvement, pre-morbid disability, major early ischemic change on NCCT, and other clinical contraindications. A further 63 patients were excluded as they had no definite acute perfusion lesion, 24 of which were subsequently identified on follow-up imaging as lacunar stroke, and the remainder having no infarction on follow-up imaging. Of the remaining 366 patients, 212 (58%) were treated with alteplase and 154 (42%) did not receive alteplase following multimodal CT at the discretion of the treating neurologist. The clinical and imaging characteristics of the patients with small perfusion lesions are shown in Table 1 and Figures 1 and 2.

The median acute NIHSS of the 366 patients with a small perfusion lesion was 8 in both treated and untreated patients (Table 1). Patients treated with alteplase had less early clinical improvement than those who were untreated (median 24 hour NIHSS 4 in alteplase patients versus 2 in untreated patients, $p=0.031$, Table 2). Of the 366 patients with a small perfusion lesion who were eligible for thrombolysis based on clinical and NCCT criteria, there was a relatively high rate of excellent outcome, 227 (62%) with mRS 0-1 at day 90. However, thrombolytic treatment did not result in a greater number of patients achieving

excellent clinical outcome (day 90 mRS 0-1, 57% alteplase patients versus 69% untreated, RR=0.83 95% CI 0.71-0.97, $p=0.022$, Figure 3). The rate of good clinical outcome was not higher for treated patients (mRS 0-2 at 90 days 72% treated patients versus 77% untreated, RR 0.93, CI 0.82-1.95, $p=0.23$).

Propensity analysis revealed that patients were more likely to be treated if they were younger, presented to hospital earlier, and had a higher NIHSS score (table 3 and supplementary figure 2). Adjusting for these variables (and other baseline variables such as baseline occlusion) using the propensity analysis identified that patients had a lower chance of having an excellent clinical outcome at 90 days with thrombolytic treatment (mRS of 0-1 RR, 0.73 CI 0.63-0.85, $p<0.001$).

Of the 366 study patients, the majority (309, 84.4%) had no acute vessel occlusion despite a perfusion deficit on CTP. Only 57(15.4%) had a baseline vessel occlusion on CTA (38 partial, 19 complete). These occlusions ranged from M2 to M3 branches of the middle cerebral artery, as well as anterior and posterior cerebral arteries. There was no significant difference between the rates of alteplase treatment in patients without a vessel occlusion (56% treated versus 44% untreated, $p=0.31$), however there was a difference in the rate of alteplase treatment in patients with an occlusion (68% treated versus 32 % untreated, $p=0.044$). Patients with a baseline vessel occlusion also had lower rates of excellent outcome with alteplase treatment (mRS 0-1 treated 45% versus untreated 55%, RR = 0.81, 95% CI = 0.62-0.97, $p=0.031$). The poorer outcomes with alteplase in patients with a baseline occlusion were not related to different recanalization rates (47% treated vs 46% untreated, $p=0.67$). In the untreated patients with recanalization there was a very high rate of excellent outcome compared to those with recanalization after alteplase (RR mRS 0-1 = 1.25, 95% CI = 1.02-1.49, $p=0.013$).

There were 10 patients with small acute perfusion lesions who had HT (3 HI1, 4 HI2, 2 PH1 and 1 PH2). Nine of the 10 patients with HT were treated with alteplase (4.2% of all treated patients, 3 HI1, 3 HI2, 2 PH1 and 1 PH2, $p < 0.001$ for any HT compared to untreated patients). Patients with HT had higher 24 hour NIHSS (median = 9, versus 4 in patients without HT, $p < 0.001$). All three patients with PH had a 90 day mRS of 4-6. Of the patients with any HT, only 2 of the 10 had a baseline vessel occlusion, and all three PH occurred in patients without an occlusion.

Discussion:

We have observed that patients with small acute perfusion lesions who were clinically eligible for alteplase had relatively high rates of good clinical outcome, irrespective of thrombolytic therapy being delivered. As might be expected, given the milder stroke severity profile in our cohort, the rates of excellent outcome were better than seen in either alteplase or placebo groups in the large randomized controlled trials.^{1,2} However, in this cohort of patients with a perfusion lesion volume of less than 15 mL, there appeared to be no net benefit from alteplase therapy. Propensity analysis did show that younger patients with higher NIHSS arriving earlier were more likely to be treated with alteplase in this cohort (Table 1). After correction for these imbalances, the likelihood of achieving an excellent clinical outcome at 90 days with thrombolysis still remained lower than patients not receiving thrombolysis. We note the imbalance in vessel occlusion status, with a significantly higher proportion of patients in the alteplase treated group having a vessel occlusion visible on CTA. This suggests clinicians may have adopted a preference for treating patients with both perfusion lesion and vessel occlusion. This study suggests that a randomised trial may be required to further elucidate the benefit or risk of intravenous thrombolysis in the patient group with a small perfusion lesion.

Contributing to the poor outcomes in the alteplase group was a significantly increased risk of HT. Although the rate of major ICH was low overall, likely reflecting the small acute ischemic lesions, this still was associated with increased rates of poor outcomes with alteplase. Furthermore, the patients in this cohort had a median acute NIHSS of 8; thereby most patients, on clinical criteria alone, would be classified as moderate in severity and very much in scope for alteplase treatment. The lack of significant therapeutic effect in this cohort suggests that perfusion lesion volume has considerably better discriminatory power for potential therapeutic response than clinical scoring alone. Finally, given the lack of benefit from alteplase in patients with a small perfusion lesion either with or without an occlusion on CTA, we suggest that neither CTA nor standard clinical/NCCT assessment can appropriately define a relatively large sub-group of patients who are clinically eligible for alteplase, yet appear to have no benefit from treatment.¹⁸

Our results contrast with the clinical outcomes for the mild stroke patient subgroup in the recent meta-analysis of the phase III alteplase RCTs.¹ In this meta-analysis, patients with mild clinical severity did appear to have a net benefit from treatment in univariate analysis. However, we note that clinical severity was not a significant predictor of outcome in multivariable analysis. Importantly, our small perfusion lesion cohort and the RCT mild stroke subgroup patient populations are not readily comparable. Perfusion imaging was not routinely collected in the phase III thrombolytic trials and the median NIHSS score of 8 indicates that many patients with small perfusion lesions in our cohort were not in the clinically 'mild' category. The pathophysiological profile of the mild stroke patients in the RCTs is unknown. It is possible that some of these patients had perfusion lesions above the 15 ml threshold and thus were more likely to benefit from alteplase.⁶ Conversely, it is possible that some patients may have had no perfusion lesion at all, given these were NCCT based trials.

We suggest it likely that the pattern of small distal perfusion lesion with no vessel occlusion indicates a group of patients who are imaged during the process of spontaneous reperfusion. The clinical corollary of this is spontaneous clinical improvement, precisely what was observed in the untreated group (median acute NIHSS = 8, median 24 hour NIHSS = 2). However, the clinical improvement appeared to lag behind the imaging, with the initially quite high acute NIHSS perhaps reflecting a more extensive perfusion deficit prior to reperfusion and CTP. It stands to reason that those with spontaneous reperfusion are unlikely to need pharmacologic enhancement of reperfusion.

The reason why patients with a small perfusion lesion and a baseline occlusion were less likely to benefit from alteplase are unclear. The rate of recanalization seen with alteplase was no higher than that in the untreated group and although there was a higher rate of HT in the alteplase treated patients, the rates of PH were not significantly different and the small absolute differences between groups suggest HT is less likely to be driving poor outcome. Alteplase has been associated experimentally with neurotoxicity due to broad-spectrum protease enzymes reaching the extracellular space following injury to the blood brain barrier from ischemia.^{19,20,21} The poorer outcomes could suggest that alteplase is inducing neurotoxicity and/or reperfusion injury (in the absence of ICH), however this is speculative. Alternate lytic agents such as tenecteplase, which show promise of an improved benefit/harm ratio, may be a better option for this group of patients (small perfusion lesions +/- vessel occlusion).^{10,22}

The main caveats when interpreting the results of this study relate to its observational non-randomized design. It remains possible that observed or unmeasured patient differences between the two groups have influenced our results. Differences between the treated and untreated patients, particularly vessel occlusion status, may have affected outcomes. This particular difference suggests the possibility of variability in practice between

individual neurologists and centres in their use of advanced CT imaging in treatment decision assistance. The propensity analysis highlighted that younger patients with higher NIHSS were more likely to be treated and correction for identified imbalances actually increased the rate of better outcomes without treatment. Lastly, it is also possible there were reasons for the variation in practice include the lack of standardization of perfusion imaging acquisition and processing across manufactures. In order to adjust for this bias the study imaging was processed centrally using a single algorithm that incorporated delay correction in order to prevent any potential overestimation of small lesion volume due to carotid stenosis or other delays in arterial filling and as such presented perfusion imaging in the delay time measure rather than the more commonly used Tmax measure. Previous studies has indicated that the DT and Tmax measure are equivalent²³ when set at a similar threshold¹⁴.

In conclusion, we have demonstrated in this observational study, that patients with small acute perfusion lesions had no observable benefit from thrombolysis with alteplase and in fact had a reduced chance of an excellent recovery. In the group of patients with a small perfusion lesion who are not candidates for endovascular therapy, there is significant justification to test alternative thrombolytic agents to improve long term patient outcomes.

Author contributions

Conception and design of the study; AB, CL, VK and MP

Acquisition and analysis of data; AB, ML, CL, VK, CX, RA, PM, LL, TK, BB, KB, ZJ, JJ, QD and MP

Drafting the manuscript or figures; AB, CL, and MP

Potential conflicts of interest

No author has any relevant conflicts to declare.

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	Alteplase treated N=212	Untreated N=154	p
Median Age (SD)	70 (14)	66 (15)	p=0.007
Hypertension	129 (61%)	79 (51%)	p=0.149
Atrial fibrillation	60 (28%)	28 (18%)	p=0.137
Diabetes	38 (18%)	39 (23%)	p=0.497
Previous stroke or TIA	51 (24%)	26 (17%)	p=0.189
Anti-thrombotic	51 (24%)	26 (17%)	p=0.297
Time from symptom onset to imaging (SD)	96 min (69)	118 min (53)	p=0.057
Median acute NIHSS (IQR)	8 (1-11)	8 (1-10)	p=0.71
Patients with any vessel occlusion	39 (68%)	18 (32%)	P=0.044

Table 1. Acute clinical characteristics of patients with a small perfusion lesion (<15 mL) who were also clinically eligible for alteplase therapy. There were no significant baseline differences between patients who were or were not treated with alteplase. IQR = interquartile range, CI = 95% confidence intervals.

	All patients N= 366	Alteplase treated N=212	Untreated N=154	p and Relative Risk
Median 24h NIHSS (IQR)	3 (0-7)	4 (0-8)	2 (1-5)	p=0.031
mRS 0-1	N=227 (62%)	N=121 (57%)	N= 106 (69%)	RR = 0.83, CI = 0.71-0.97 p=0.022
mRS 0-2	N= 271 (74%)	N= 152 (72%)	N= 119 (77%)	RR = 0.93 CI = 0.82-1.95 p=0.23
mRS 5-6	N= 9 (2%)	N= 7 (1.6%)	N= 2 (0.4%)	RR = 2.66 CI = 1.1-12.2 p=0.036
Median acute perfusion volume (IQR), mL	3 (1-11)	3 (1-10)	4 (1-11)	p=0.61
Any HT	10 (2.3%)	9 (2%)	1 (0.3%)	p<0.001
PH	3 (0.7%)	3 (0.7%)	0	NA

Table 2. Follow-up clinical characteristics of patients with a small perfusion lesion (<15 mL) who were also clinically eligible for alteplase therapy. There were no significant baseline differences between patients who were or were not treated with alteplase. IQR = interquartile range, RR = Relative Risk, CI = 95% confidence intervals.

Predictors of treatment with thrombolysis in the INSPIRE registry for patients with an acute perfusion lesion < 15mL

Baseline predictors of receiving thrombolysis	Odds ratio (95% confidence interval)	P
Sex	0.861 (0.54-1.39)	0.557
Age	0.969 (0.95-0.98)	<0.001
Baseline occlusion	1.519 (0.79-3.02)	0.233
Acute NIHSS	1.146 (1.06-1.12)	<0.001
Onset to door time	1.009 (1.00-1.01)	<0.001
Centre (John Hunter Hospital vs <i>other centres</i>)	5.03 (0.78-32.14)	0.088
Adjusted relative risk (weighted logistic regression)		
mRS 0-1	0.73 CI 0.63-0.85	<0.001

Table 3. Propensity analysis results assessing baseline variables that may have influenced the probability of treatment with thrombolysis for patients with an acute perfusion lesion of <15mL. Centre dichotomized to JHH vs other centres. Younger age, higher acute NIHSS and later time of arrival were significant predictors of patients receiving thrombolysis. After adjustment and weighting of these influences from the propensity analysis, the results of this analysis suggest that patients treated with thrombolysis were less likely to achieve an excellent outcome at 90 days.

Site	Scanner	Acquisitions	Contrast	Axial coverage
John Hunter Hospital	Aquilion 320-slice CT scanner (Toshiba)	19 acquisitions in 60 seconds	Forty mL of contrast (Ultravist 370) at 6 mL/s, followed by 30 mL of saline	160mm
Royal Adelaide Hospital	Definition AS+ (Siemens)	19 acquisitions in 60 seconds	Forty mL of contrast (Ultravist 370) at 6 mL/s, followed by 30 mL of saline	96mm
Queen Elizabeth Hospital	Aquilion 320-slice CT scanner (Toshiba)	19 acquisitions in 60 seconds	Forty mL of contrast (Ultravist 370) at 6 mL/s, followed by 30 mL of saline	160mm
Gosford Hospital	64 detector lightspeed (General Electric Healthcare)	19 acquisitions in 54 seconds	Forty five mL of contrast agent (Ultravist 370) was injected at 6 mL/s.	80mm (40*2)
Huashan Hospital	Brilliance iCT 128-slice (Philips)	23 acquisitions in 60 s	Forty mL of contrast agent (Ultravist 370) was injected at 5 mL/s, followed by 20 mL saline	125mm
Second Affiliated Hospital of Zhejiang University	Definition Flash dual source CT (Siemens)	10 acquisitions in 60 seconds	Fifteen mL of contrast agent (Ultravist 370) was injected at 4mL/s followed by 20mL of saline	100mm
Sunnybrook Medical Center	Lightspeed (GE Healthcare)	6 acquisitions in 135 seconds	0.7 mL/kg iodinated contrast agent up to a maximum 90 mL (Omnipaque 300 mg iodine/mL);	41mm

Supplementary Table 1. The acute CTP acquisition parameters for each site involved in this study from the INSPIRE acute perfusion registry. All imaging took less than 10 minutes to perform on all patients.

Figure 1. Patient flow chart. We utilized the INSPIRE database which contains 1562 cases with complete clinical and advanced imaging information, including acute CTP. In the registry, 531 patients had an acute perfusion lesion of $<15\text{mL}$, as pre-specified for the analysis. Of these 531 patients, 165 were excluded from the study and a total of 366 patients were assessed. Of the 366 patients 212 received thrombolysis and 154 did not.

Figure 2. Identification of small perfusion lesions with post processed imaging. The first 5 columns show standard outputs from MISTar software (CBF and CTA source images). The last column shows the post processed images that have applied a threshold (delay time >3 seconds) to identify ischemic tissue for this study. Patients with an ischemic lesion of $<15\text{mL}$ were analysed for this study.

Figure 3. mRS distribution of ischemic stroke patients with a small perfusion lesion ($<15\text{mL}$), who were or were not treated with alteplase.

Figure 1. Patient flow chart. We utilized the INSPIRE database which contains 1562 cases with complete clinical and advanced imaging information, including acute CTP. In the registry, 531 patients had an acute perfusion lesion of <15mL, as pre-specified for the analysis. Of these 531 patients, 165 were excluded from the study and a total of 366 patients were assessed. Of the 366 patients 212 received thrombolysis and 154 did not.

233x226mm (300 x 300 DPI)

Figure 2. Identification of small perfusion lesions with post processed imaging. The first 5 columns show standard outputs from MISTar software (CBF and CTA source images). The last column shows the post processed images that have applied a threshold (delay time >3 seconds) to identify ischemic tissue for this study. Patients with an ischemic lesion of <15mL were analysed for this study.

175x171mm (300 x 300 DPI)

AC

Figure 3. mRS distribution of ischemic stroke patients with a small perfusion lesion (<15mL), who were or were not treated with alteplase.
243x131mm (300 x 300 DPI)

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Author/s:

Bivard, A;Lou, M;Levi, CR;Krishnamurthy, V;Cheng, X;Aviv, RI;McElduff, P;Lin, L;Kleinig, T;O'Brien, B;Butcher, K;Zhang, J;Jannes, J;Dong, Q;Parsons, MW

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