Whole-brain CTP in acute ischemic stroke

by

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DECLARATION

I Longting Lin hereby declare that the thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968.

I Longting Lin hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications.

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PUBLICATIONS, PRESENTATION, AND AWARDS

Peer reviewed publications included in this thesis:

- Lin L, Bivard A, Parsons MW. Perfusion patterns of ischemic stroke on computed tomography perfusion. J Stroke. 2013 Sep; 15(3):164-73.

- Lin L, Bivard A, Levi CR, Parsons MW. Comparison of computed tomographic and magnetic resonance perfusion measurements in acute ischemic stroke: back-to-back quantitative analysis. Stroke. 2014 Jun; 45(6):1727-32

- Lin L, Bivard A, Krishnamurthy V, Levi CR, Parsons MW. Whole-brain CT perfusion measures the acute infarct core and penumbra accurately and precisely (Submitted to Radiology, RAD-15-0319)

- Lin L, Bivard A, Levi CR, Parsons MW. Reperfusion on Tmax Map Best Predicts Clinical Outcome of Stroke (submitted)

Conference presentations arising from this thesis:

- Lin L, Bivard A, Kemp D, Parsons MW, Levi CR. Comparison of perfusion CT and MR in hyperacute stroke. Paper presented at the Proceedings of the 23rd Stroke Society of Australasia Annual Scientific Meeting/ the 8th Smart Strokes Australasian Nursing and Allied Health Stroke Conference, Sydney, NSW, Australia; August 2012. Abstract published in International Journal of Stroke, Vol. 7 (Suppl.1), Page 14 (Session G.1).

- *Lin L*, Bivard A, Krishnamurthy V, Levi C, Parsons M. Whole-brain CT perfusion measures the acute ischemic lesion accurately and precisely. Paper presented at the Proceedings of the 25th Annual Scientific Meeting of the Stroke Society of Australasia, Hamilton Island, Queensland, Australia; July 2014. Abstract published in International Journal of Stroke, Vol. 9 (Suppl.1), Page 25 (Free Papers 7).

- Lin L, Bivard A, Krishnamurthy V, Levi C, Parsons M. Comparison of Whole-Brain CTP and Limited-Coverage CTP. Paper presented at the Proceedings of Asian Pacific Stroke Conference, Taipei, Taiwan; September 2014. Abstract published in Cerebrovascular Diseases, Vol. 38 (Suppl.1), Page 2 (F01-4).

- Lin L, Bivard A, Levi C, Parsons M. How to Measure Cross-Modality Reperfusion with Acute CTP and 24-Hour MRP. Paper presented at the Proceedings of Asian Pacific Stroke Conference, Taipei, Taiwan; September 2014. Abstract published in Cerebrovascular Diseases, Vol. 38 (Suppl.1), Page 12 (F03-7).

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- Bivard A, Lin L**,** Parsons MW. Review of stroke thrombolytics. J Stroke. 2013 May; 15(2):90-8.

- Lin L, Parson M. Assessment of collaterals in acute stroke using dynamic CT angiography. Paper presented at the Proceedings of the 16th National conference of Neurology (OR070), Nanjing, China; October 2013.

- Campbell BC, Christensen S, Yassi N, Sharma G, Bivard A, Lin L, Levi CR, Desmond PM, Donnan GA, Straka M, et al.. Comparison of Automated Whole Brain CT Perfusion Analysis with Perfusion-Diffusion MRI in Ischemic Stroke. Paper presented at the Proceedings of the American-Heart-Association/American-Stroke-Association International Stroke Conference / Nursing Symposium, Honolulu, HI; February 2013. Abstract published in Stroke, Vol. 44, AWP45.

- Yassi N, Campbell BC, Christensen S, Sharma G, Bivard A, Lin L**,** Levi CR, Desmond PM, Donnan GA, Davis SM, et al.. Reduced Cerebral Blood Flow on Acute Whole Brain CT Perfusion Best Predicts Hemorrhagic Transformation. Paper presented at the American-Heart-Association/American-Stroke-Association International Stroke Conference / Nursing Symposium, Honolulu, HI; February 2013. Abstract published in Stroke, Vol. 44, AWP33.

Statement by co-authors for the paper:

Lin L, Bivard A, Levi CR, Parsons MW. Comparison of computed tomographic and magnetic resonance perfusion measurements in acute ischemic stroke: back-to-back quantitative analysis. Stroke. 2014 Jun; 45(6):1727-32

As co-authors of the paper, we confirm that Longting Lin is the primary contributor to the publication. Longting Lin has made following contributions:

- 75% design of the research
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ABSTRACT

Perfusion imaging technology not only enables stroke diagnosis by identifying the ischemic lesion earlier, but also helps the clinician to make treatment decisions by further classifying the ischemic lesion into salvageable tissue and non-salvageable tissue. The imaging of salvageable tissue, penumbra, provides a direct target for reperfusion treatment. However, the accuracy of penumbra measurement with perfusion imaging has been questioned, especially with CT perfusion (CTP). Perfusion images, acquired on earlier generation instruments such as the16 or 64-detector scanners, have limited coverage of potentially ischemic brain, a factor recognised to reduce the accuracy of penumbra measurement. This limitation can be overcome by the advance in technology. The new generation "mega-detector" scanners, such as 320-detector Toshiba Aquilion One, provide whole brain coverage of 160mm from skull base to vertex. In this thesis, I presented a series of studies aiming to evaluate the utility of whole-brain CTP in acute ischemic stroke.

The first study was to derive the optimal penumbra measurement on whole-brain CTP with the reference of ischemic tissue outcome, and the second study was to test the penumbra measurement of whole-brain CTP in predicting clinical patient outcome. The two studies found that only with the threshold setting at Tmax>6s or DT>3s, did the whole-brain CTP achieve high accuracy (>99%) in delineating acute ischemic penumbra and good sensitivity (>80%) in predicting favourable clinical outcome. It was also confirmed that the accuracy of penumbra measurement was comprised when the brain coverage of CTP decreased from 160mm to 20mm.

Following two studies examined the utility of whole-brain CTP in the clinical setting. Firstly, CTP was compared to MRP, the perfusion modality that has already been well used in clinic. This work demonstrated that with whole brain coverage, CTP was as effective as MPR in

measuring the acute penumbra and in selecting patients for reperfusion treatment. Secondly, a case by case review was carried out to assist clinicians in the interpretation CTP output.

In conclusion, findings of this thesis support the usage of whole-brain CTP in acute ischemic stroke. Noticeably, the conclusion only applies to patients with anterior circulation stroke. Whole-brain CTP might also have advantage in detecting ischemic lesions in posterior circulation territory, which require studies to prove it in the future.