# Aqueductal Flow Measurement in a Rat Model of Communicating Hydrocephalus using Gadolinium Enhancement

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## ABSTRACT

We recently demonstrated the measurement of pulsatile aqueductal flow in the rat in intact controls and experimentally induced hydrocephalus animals [1]. These experiments a showed marked increase in the pulsatile flow stroke volume in the hydrocephalic animals. However, the demonstration of pulsatile flow in control, with much reduced stroke volumes, results in very noisy waveform in which we were able to reliably measure stroke volume in less than 50% of the animals. In this work, we have used an intraventricular injection of Gadolinium in order to boost the MR signal intensity and demonstrate reliable measurement of pulsatile aqueductal flow.

## INTRODUCTION

Research, clinical evaluation and the treatment of hydrocephalus is mostly focused on the bulk flow of CSF out of the ventricular system. Within the last ten years, MRI flow techniques have been used to show that the pulsatile flow of CSF is important as well, and hyperdynamic pulsatile flow in the aqueduct can often be used as a predictor of successful shunt outcome. We have recently developed two new models of communicating hydrocephalus in the rat, which have the potential of being used to elucidate the biochemical and biomechanical basis of ventricular dilation. With these new models we will begin to explore the entire time course of the disease from the acute to the chronic stages.

In order to follow the time course of changes in ventricular pulsations, accurate measures must be attainable in all animals even in the acute stages when pulsations may be normal. While our initial investigations showed that normal aqueductal pulsations could be detected, we have since determined that this was only true in the minority of cases, with aqueductal pulsatility being hidden in the background phase noise in most cases. Based on the expected normal aqueductal stroke volume (5 – 15 nl), it was estimated that close to 1 hour of imaging time would be required to obtain adequate pulsatile flow waveforms. To obviate a lengthy imaging session, we hypothesized that it would be possible to measure aqueductal flow reliably by using an intraventricular injection of Gadolinium in order to enhance the MR signal in the aqueduct.

## METHODS

Five rats (280 – 360 g) were anesthetized with nembutol (40 mg/kg) and secured in a stereotactic head holder. A small 0.75 mm diameter burr hold was drilled into the skull just down to the surface of the dura at -0.9mm posterior and +1.5 mm lateral to Bregma. A 30G needle was then inserted into the ventricle at a depth of 3.6mm. Gadolinium (Magnevist, Berlex Labs, NJ) diluted 1:20 in sterile saline was then infused into the ventricle at a rate of 5-10 µl/min, with a total injected volume of 20-30 µl. The needle was then slowly removed from the cranium, the burr hole was then sealed with cyanoacylate glue and the skin tied closed. The animal was then inserted into a 9.4T Bruker Avance scanner. Imaging included 3D SPGR with TE/TR = 4/12 ms, FA 20˚, FOV 3 cm, matrix 256 x 192, ST 0.4 mm in order to visualize the gadolinium enhancement. Flow imaging through the cerebral aqueduct used a gradient echo phase contrast sequence with the following parameters: TE/TR = 6/10 ms, FA 5-40˚ (depending on Gd dose), FOV 3 cm, matrix 128 x 128, ST 1 mm, Venc = 1 cm/s (positive and negative encoding sequences were run separately and subtracted), and retrospective gating on the peripheral pulse obtained from the hindpaw, with 16 frames reconstructed. Flip angle was optimized in each case for the amount of gadolinium in the aqueduct at the time of imaging. Images were processed off-line with custom-built Matlab (The Mathworks, Natick, MA) software. Stroke volume was calculated by summing all pixels in the aqueduct and integrating flow waveforms over all positive values.

## RESULTS

Four animals demonstrated adequate enhancement in the CSF. For one animal, a long delay (about 1.5 hour) between injection and flow imaging lead to inadequate CSF enhancement and no measurable aqueductal flow. In the other four animals, three demonstrated measurable flow. Figure 1 shows a magnitude and phase images in one animal, showing enhancement of the cerebral aqueduct as well as the subarachnoid spaces. Figure 2 shows the associated flow waveform. Stroke volume in these animals was 14.0±2.7 nl (range 12.3–17.0 nl). The noisy flow waveform from a non-gadolinium rat is shown for comparison.

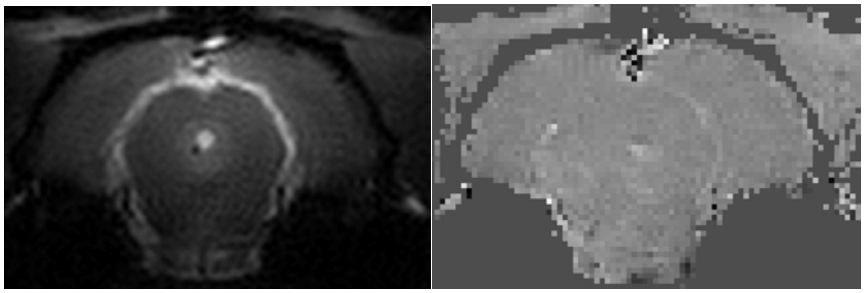

Figure 1: Magnitude and phase flow images of the cerebral aqueduct in a rat, after an intraventricular injection of gadolinium to enhance the CSF visibility.

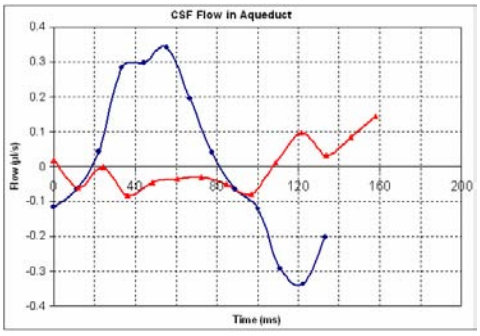


Figure 2: Flow waveform with (blue) and without (red) a gadolinium injection.

## CONCLUSIONS

We have demonstrated enhancement of the signal in the cerebral aqueduct and a significant improvement in the measurement of the pulsatile stroke volume out of the ventricular system. This technique will allow the reliable and reproducible measurement of pulsatile flow in both intact control animals as well as over the course of the development of ventricular dilation in hydrocephalus rat models.

References

1. M. Wagshul, *et al*, Proc. ISMRM, Seattle, WA, 2006.

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