



X-ray phase contrast imaging of the whole brain *in situ*: from traumatic to diffuse white matter injury

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INTRODUCTION

Our interdisciplinary collaboration aims to spatially resolve brain injuries that currently elude existing clinical imaging modalities, including both traumatic and diffuse injury, to improve our understanding of the progression of cerebral palsy near birth.

OBJECTIVES

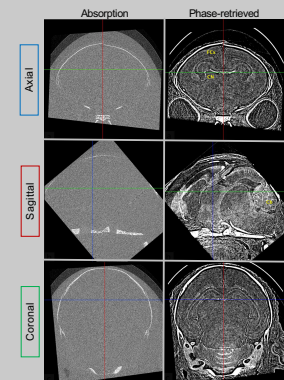
- Aim 1: To develop novel PC-CT technologies for early and accurate diagnosis of diffuse white matter injury.
- Aim 2: To develop super-resolution PC-CT for measuring cellular-level damage in brain tissue.
- Aim 3: To develop a compact PC-CT system for pre-clinical and clinical brain imaging.

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METHODOLOGY

HIGH SPATIAL/CONTRAST RESOLUTION

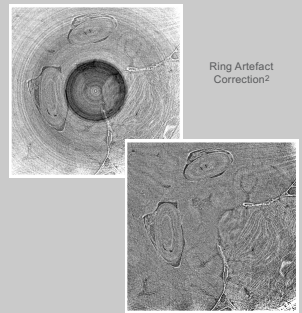
Use PC-CT to resolve grey/white matter structures within the brain *in situ* at both high spatial and high contrast resolution¹.



NEW TECHNIQUES

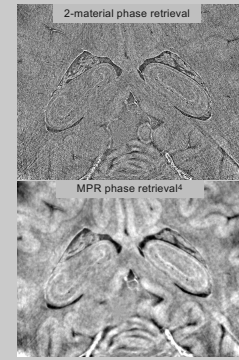
Develop novel techniques to overcome artefacts, improve resolution, and reduce X-ray dose, and translate these methods for laboratory sources.

Validate new methods using imaging phantoms and/or simulations.



DIFFUSE WHITE MATTER INJURY

Apply the methods developed to resolve diffuse white matter injury² that cannot be resolved with conventional methods, using a Fetal Growth Restriction (FGR) model.



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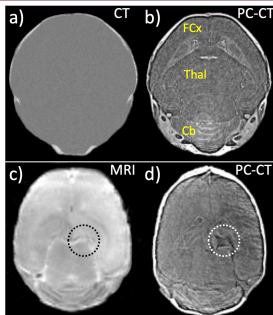
RESULTS

Rabbit kitten brains imaged with a) conventional CT and b) our PC-CT (32 μ m resolution; 5 min scans).

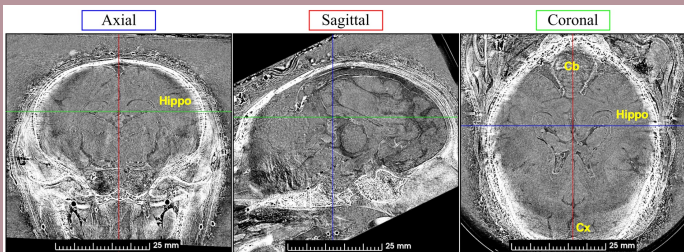
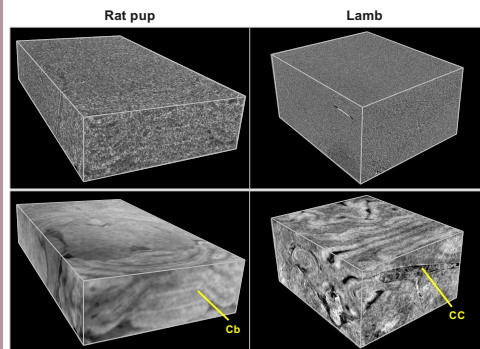
Rat brain with severe brain injury (hypoxic-ischemic; dotted circles) imaged with c) 9.4 Tesla MRI (T2, 125 μ m resolution; 44 min scan); d) our PC-CT (37 μ m resolution, 5 min scans).

Brain region key:
Cx = Cortex; FCx = Frontal Cortex; Thal = Thalamus; Cb = Cerebellum; Hippo = Hippocampus

1. Croton et al., 2018, *Sci Rep*; 2. Croton et al., 2022, *Proc. Of SPIE*.



Volume renderings PC-CT volumes of regions within the brains of a rat pup (left) and a lamb (right) before (top) and after MPR phase retrieval⁴ (bottom)



*PC-CT images from fetal sheep brain within the skull shown in axial (blue), sagittal (red) and coronal (green) plane. The crosshairs on each image correspond to the locations of the slices from the other planes.

Project topics:

- X-ray phase contrast CT
- Micron-scale neuroimaging
- Direct detection of diffuse brain injury
- High-sensitivity image artefact correction
- Biomedical applications of phase contrast imaging
- Dose reduction and multi-scale imaging

04 DISCUSSION

→ Early detection of perinatal brain injury is challenging with existing brain imaging methods, particularly when the neuropathology is diffuse or subtle.

→ Magnetic resonance imaging (MRI) is expensive, scan times are long, and has poor spatial resolution.

→ Conventional computed tomography (CT) scans are faster, have higher spatial resolution but provide poor contrast of brain structures.

→ We have previously demonstrated that phase contrast x-ray imaging CT (PC-CT) can detect traumatic brain injury and hypoxic-ischemic brain injury *in situ* (rabbit kittens and rat pups) at both high spatial and high contrast resolution.

→ We have overcome imaging ring artefacts due to the highly absorbing skull using our newly developed image processing techniques to successfully obtain high-resolution images of control preterm fetal sheep brains *in situ*.

→ These PC-CT images allow us to clearly visualise structures within the brain inside a preterm fetal sheep skull down to ~36 μ m in size.

→ Images collected from preterm fetal sheep provide the groundwork for future application of our techniques for detecting diffuse perinatal brain injury.

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CONCLUSION

This project employs PC-CT. Standard CT derives image contrast from attenuation of X-rays as they pass through an object. Phase contrast imaging derives added contrast from refraction and diffraction. By introducing phase contrast via propagation-based imaging, we can mathematically retrieve material boundaries using PC-CT that are unresolved with attenuation alone.

PC-CT is an emerging modality that offers both high image contrast and high spatial resolution. However, it is still in its infancy with respect to clinical translation. This project will build on recent achievements, overcoming the technical obstacles to image more human-like brains, reduce X-ray dose, and apply newly developed methods for preclinical research. Future work will build even further on these achievements to work toward the long-term goal of clinical translation.

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1. LCP Croton, KS Morgan, DM Paganin, LT Kerr, MJ Wallace, KJ Crossley, SL Miller, N Yagi, K Uestugi, SB Hooper, & MJ Kitchen, *In Situ Phase Contrast X-ray Brain CT*, *Sci Rep*, 8, 11412 (2018)
2. LCP Croton, G Ruben, KS Morgan, DM Paganin, & MJ Kitchen, Ring Artefact Suppression in X-ray Computed Tomography Using a Simple, Pixel-wise Response Correction, *Opt Express*, 27 (10), 14231 (2019)
3. LCP Croton, KJ Crossley, Pre-clinical phase-contrast imaging of the whole brain *in situ*, from traumatic to diffuse white matter injury, *Developments in X-Ray Tomography XIV*, 12242, (122421B) (2022)
4. JA Pollock, LCP Croton, KS Morgan, KJ Crossley, MJ Wallace, GA Buckley, SB Hooper, & MJ Kitchen, 3DMPRe—a robust morphological approach for applying phase retrieval in proximity to highly attenuating objects in computed tomography, *J Synchrotron Radiat*, 32, 5, 1319-1327 (2025)

