INTRODUCTION

High-resolution, post-mortem MRI provides stunning structural images of cerebral anatomy that are not possible in vivo due to motion and rapid imaging artifacts.

The reliability and accuracy of post-mortem diffusion tensor imaging (DTI) measurements are not well understood, in part due to the unknown effects of fixation on the brain’s diffusion properties.

In animal studies, peri-mortem perfusion fixation alters mean diffusivity (MD), but leaves fractional anisotropy (FA) relatively unaffected [1,2].

In human studies, immersion fixation has led to generally poor quality DTI contrasts [3,4].

Routine post-mortem processing typically involves 24 to 48 hours post-mortem delay before fixation begins. Additionally, brain dead and cerebral ischemia patients are common donors, which may involve an additional 24 to 72 hours of pre-mortem cessation of cerebral vascular perfusion. Because neural tissue degrades relatively quickly in situ and ex vivo without fixation, DTI contrast is largely lost in these subjects. In cases of highly motivated donors — e.g., those with a terminal condition and a status of “do not resuscitate” and “do not intubate” — it is possible to acquire DTI data within a much shorter time period. But how soon is “soon enough”?

We use a porcine model to study the acute time course (<18 hours) of neural tissue degradation and response to immersion fixation to enable the design of rapid protocols for post-mortem DTI studies.

Methods

Intact cerebra were removed from two porcine specimens (~25 kg, 3-4 months) ~1 hour post-mortem.

**Degradation Study**

- 1 Pig
- 1 Pig
- Lactated Ringers
- Fixation
- 13 Hours
- Post-mortem
- PM
- H&E
- WM, GM
- Diffusion
- In Vivo
- Post-Mortem
- 14 hours
- DWI

**Delayed Fixation Study**

- 1 Pig
- Lactated Ringers
- Fixation
- 1 Hour
- Post-mortem
- PM
- H&E
- WM, GM
- Diffusion
- In Vivo
- Post-Mortem
- 14 hours
- DWI

RESULTS

**Degradation Study**

(No fixation, between 13-17 h post mortem)

- FA decreased by 0.05 [FA] (9.0%) in WM and 0.02 [FA] (6.2%) in GM.
- MD decreased by 0.08 x 10^-3 mm^2/s (14.3%) and 0.04 x 10^-3 mm^2/s (0.6%).

**Delayed Fixation Study**

(Immersion fixation between 1 and 13 h)

Impacts of Fixation

- Fixation resulted in a mean FA decrease of ~35% in WM and ~30% in GM and mean MD decrease of ~51% in WM and ~56% in GM relative to the scan of non-fixed tissue of the same post-mortem time point.

**Summary**

The within tissue compartment decrease in SNR with delayed fixation indicates that the changes in MD and FA are not uniform, which suggests increasingly uneven tissue degeneration over time, even with a short (13 hour) period. Delaying fixation negatively impacts the achievable FA contrast to noise ratio through (1) overall loss of diffusivity, (2) increased loss of diffusivity in WM relative to GM, and (3) increased intra-tissue compartment variability.

CONCLUSION

- DTI contrasts are well preserved during a “window” of 6-10 hours post-mortem.
- During this period:
  - High resolution, post-mortem DTI will likely succeed without fixation.
  - The relationships between the parallel and perpendicular diffusivities of GM and WM are relatively intact.
- The observed dependence of DTI contrasts on post mortem delay could explain the variability of previous studies investigating ex vivo human imaging.
- In the acute time period, degeneration more severely impacted parallel diffusivity, which may be indicative of primary axonal degeneration with relative sparing of myelin integrity.

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**REFERENCES**