Background
Around 40% of patients with frontotemporal dementia (FTD) have tau-positive inclusions at post-mortem with a variety of different pathologies found, named primary tauopathies. Unique conformations of tau are hypothesized to underlie the distinct morphological and cellular distribution of pathological tau aggregates. In this study we investigated the potential of a set of antibodies (Fig 1) targeting the whole length of the tau protein to detect the different conformational changes in the primary tauopathies (Fig 2). The aim of the work was to identify distinct conformational changes that could be detected with specific antibodies and facilitate a post-mortem diagnosis for the pathology.

Methods
Brain tissue from twenty cases of primary tauopathy from the Queen Square Brain Bank (QSBB), London, UK were assessed (Table 1): five each with Pick’s disease (PSP), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and two with glial tauopathy (GTT) as well as five cases of Alzheimer’s disease for comparison. Eight µm sections from paraffin wax blocks of brain tissue from the frontal cortex, temporal cortex and hippocampus of each case were selected. Ten different antibodies were used: four targeting the N-terminal (tau 123, tau 12, HT7 and 7E5), three targeting the proline-rich domain (BT2, tau 224 and IG2) and two targeting the C-terminal (tau 368 and K91A) (Fig 1).

Results
Results show that individual antibodies selectively bind to specific tauopathies whilst staining negative to others, confirming a distinct fibril organisation for each tauopathy. Comparing all results to the gold standard for staining of tau pathological inclusions (using AT8 antibody), N-terminal antibodies mostly stained PiD inclusions and PSP astrocytic plaques. Antibodies targeting the proline-rich domain of tau, positively stained the pathological inclusions present in AD, PSP, PiD and GGT although tau 224 stained pathological tau in all pathologies. Finally, C-terminal antibodies positively bound to astrocytic inclusions present in CBD and PSP.

Conclusions
Here, we report the potential of several tau antibodies to selectively bind to specific forms of tauopathy.