

|                                       |   |
|---------------------------------------|---|
| <b>Names</b> (Presenter in bold font) | <b>Gina Richter-Stretton</b> <sup>1</sup> , Gerhard Leinenga <sup>1</sup> , Wendy Lee <sup>1</sup> , Matthew Pelekanos <sup>1</sup> , Jae Song <sup>1</sup> , Antony Chicoteau <sup>1</sup> , Soo Lee <sup>1</sup> , Felicia Coleman <sup>1</sup> , Caitlin McElligott <sup>2</sup> , Anthony Harris <sup>3</sup> , Henry Beale <sup>3</sup> , Jason Mattingley <sup>3</sup> , Peter Nestor <sup>1,2</sup> , Rachel De Las Heras <sup>1</sup> , Jürgen Götz <sup>1</sup>  |
| <b>Affiliations</b>                   | <sup>1</sup> Clem Jones Centre for Ageing Dementia Research (CJCADR), Queensland Brain Institute (QBI), University of Queensland, St Lucia, QLD Australia<br><sup>2</sup> Mater Research, Memory and Cognitive Disorders Clinic, South Brisbane, QLD Australia<br><sup>3</sup> Queensland Brain Institute (QBI), University of Queensland, St Lucia, QLD Australia  |
| <b>Title</b>                          | Scanning ultrasound translation   |
| <b>Abstract</b> (max 300w)            | Scanning Ultrasound (SUS) is a potential therapeutic modality for brain diseases that has its foundation in our preclinical work in mice and sheep. Complemented by test bed studies, a non-invasive, bespoke ultrasound device was built and is currently being explored in a safety trial in Alzheimer’s Disease (AD) patients (ACTRN12622000827730). Mouse studies using three complementary SUS modalities (SUS <sup>only</sup> for neuromodulation, SUS with intravenously injected microbubbles [SUS <sup>+MB</sup> ] for blood-brain barrier opening [BBBO], and SUS with intravenously injected microbubbles for delivery of monoclonal antibodies [SUS <sup>+MB+mAb</sup> ]) collectively achieved improved memory function, improved motor functions, and the clearance of amyloid plaques and tau tangles associated with AD. Sheep were used as a large animal model to address the scaling problem in human translation, including increased skull thickness and brain size, and to establish the clinical procedure. A safety trial has been initiated using the SUS <sup>only</sup> paradigm in human study participants with AD. The trial is run in an outpatient setting across four treatments and uses a bespoke 286 kHz ultrasound system with image guided navigation to treat a large area of the brain. Further device development and preclinical animal studies will go into follow-up clinical trials. |