

Assessment of the thymus in fetuses prior to spontaneous very preterm birth using functional MRI

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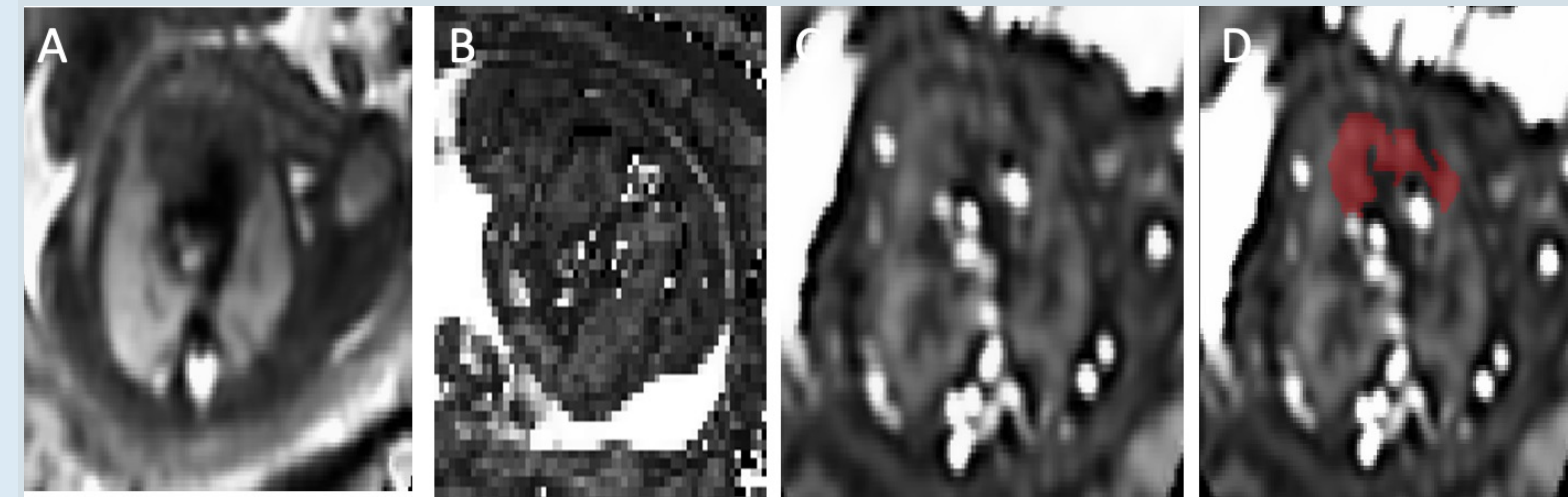


Figure 1: Summary of methodology: A) T2 image; B) T2* echo prior to alignment; C) T2* map following alignment to the T2 image; D) T2* map with segmentation of fetal thymus avoiding major vasculature.

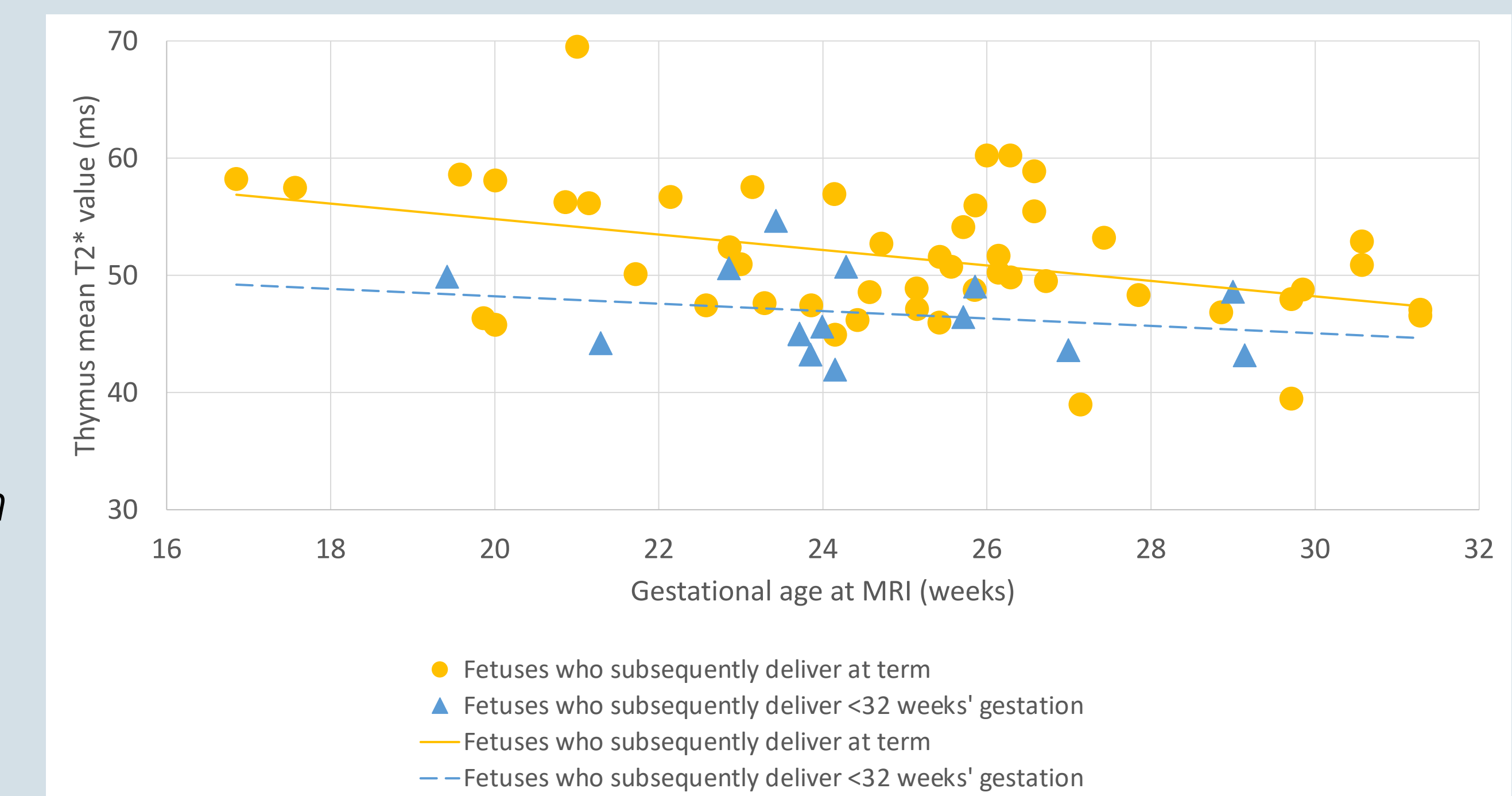


Figure 2: Mean thymus T2* decreases across gestation ($p < 0.001$) and is lower in cases than in controls ($p < 0.001$).

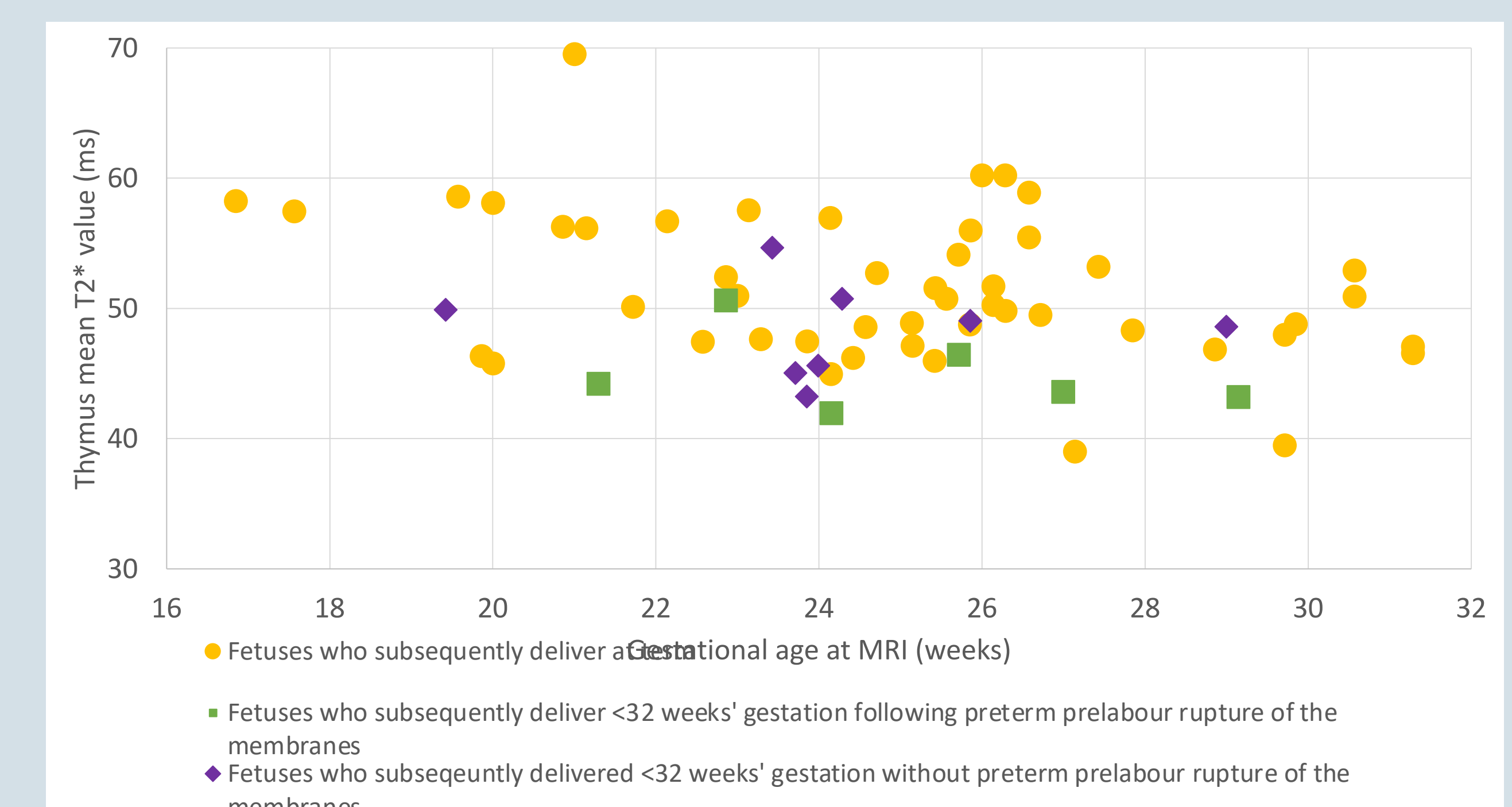


Figure 3: Mean thymus T2* is more affected in the PPROM group ($p=0.002$) than the membranes intact group ($p=0.067$).

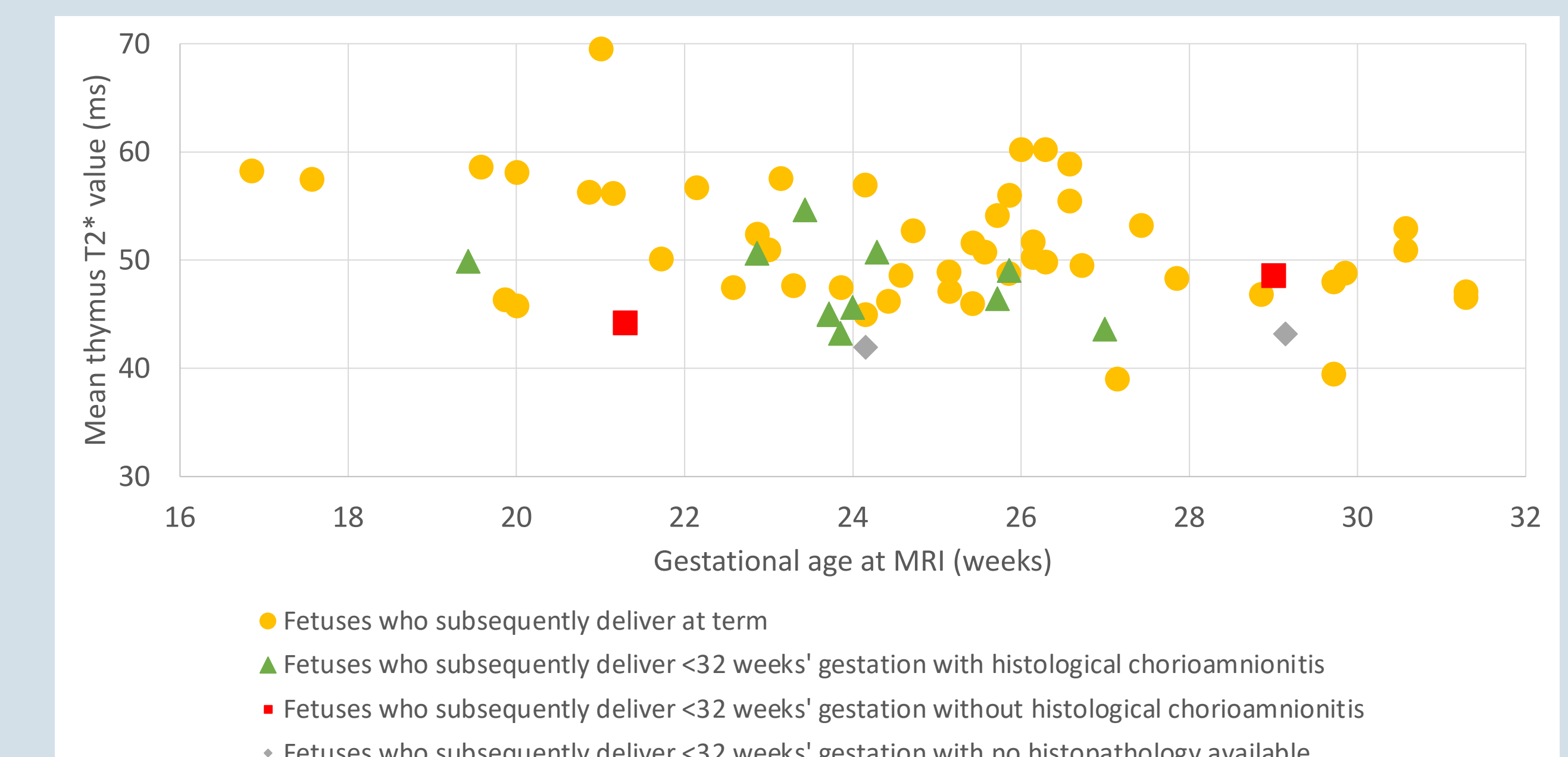


Figure 4: Impact of placental histopathology on mean thymus T2*.

Introduction

Spontaneous preterm birth complicates ~7% of pregnancies and is the leading cause of neonatal mortality and long-term morbidity globally. Although the exact aetiology is uncertain and likely multifactorial, infection is strongly implicated particularly at earlier gestations. Alterations in the fetal thymus, a gland known to be integral to the fetal inflammatory response, have been documented in fetuses who subsequently deliver spontaneously preterm, although *in vivo* assessment has been limited to volumetry. Advances in fetal MRI now allow for functional assessment of fetal tissues, including by T2* relaxometry which gives an indirect assessment of fetal oxygenation.

Objectives

1. Determine normal trends in fetal thymus volume across gestation;
2. Compare mean fetal thymus T2* in a group of uncomplicated pregnancies and those that subsequently deliver prior to 32 weeks' gestation;

3. Consider the impact of PPROM and placental histology on results.

Methods

Women were recruited who were deemed to be at very high risk of delivery prior to 32 weeks' gestation and retrospectively excluded if they did not deliver prior to this gestation. A control group of women with low-risk pregnancies were recruited and retrospectively excluded if they developed any pregnancy related complications after scanning. All women underwent a fetal MRI scan on a 3T system incorporating the fetal thorax. T2 and T2* data were aligned and the mean T2* of the thymus tissue determined (Figure 1).

Results

Mean thymus T2* decreased with gestation in control fetuses. ($p < 0.001$) (Figure 2). In fetuses who went on to deliver prior to 32 weeks' gestation, thymus volume was reduced as was mean T2* ($p < 0.001$) as compared to controls (Figure 2). On subgroup analysis, this relationship persisted for among cases affected by PPROM ($p=0.002$)

than those with intact membranes ($p=0.067$) (Figure 3). Given the high rates of chorioamnionitis in the cases we were unable to provide a meaningful comparison for the impact of this (Figure 4).

Discussion

This pilot study has successfully demonstrated a reduction in thymus mean T2* value in fetuses who go on to deliver extremely preterm. This is likely secondary to the reduced oxygenation associated with thymic involution and T-cell depletion that occurs secondary to inflammation and infection. The application of T2* imaging for *in vivo* assessments of the fetal thymus opens a new frontier for understanding the complex antenatal immunological changes linked to preterm birth. While the study has its limitations, it sets the stage for future research that integrates imaging data with cellular and molecular markers, such as T-cell analyses from cord blood, to paint a more complete picture of fetal immune health and its potential long-term ramifications.