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Brain matters in twin-twin transfusion syndrome

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Aim and outline of the thesis

The aim of this thesis is to provide insight into the risks of fetal and neonatal brain injury and long-term neurodevelopmental impairment in survivors of TTTS in the era of fetoscopic laser surgery.

This thesis is divided into six parts. You are now reading the first part, consisting of the general introduction and aim and outline of the thesis.

In part two, *chapter 1* provides a review of the literature summarizing the latest insights into TTTS. It covers prenatal management, as well as fetal and neonatal complications, with extra attention for cerebral injury and long-term neurodevelopmental impairment.

The third part of the thesis explores brain injury in TTTS treated with fetoscopic laser surgery. In *chapter 2*, we describe the incidence and risk factors of severe cerebral injury in a large case-control study of TTTS survivors, compared to a control group of dichorionic twins who were matched for gestational age. When we proceed to *chapter 3*, an even larger consecutive cohort is described where we investigate which different types of brain injury occur in fetuses and neonates with TTTS. We also describe the neurodevelopmental outcome of survivors with fetal or neonatal brain injury and review the use of different modalities for neuroimaging in our fetal therapy center.

The focus in the fourth part is on long-term neurodevelopment after TTTS. In *chapter 4*, we compare the neurodevelopmental outcome, measured using a standardized test at the corrected age of two years, between a recent cohort and an earlier cohort of TTTS survivors treated with laser surgery to investigate whether there is still room for improvement. Because studies in recent years have shown a marked decrease in fetal and neonatal mortality and morbidity in TTTS, we introduce mild neurodevelopmental impairment as an outcome measure. We dive deeper into the more subtle impairments in *chapter 5*, which is the description of a study of behavioral outcome after fetoscopic laser surgery for TTTS.

In part five, we explore a possible cause of the sometimes large differences in reported mortality and morbidity rates in TTTS between fetal therapy centers across the world. We do this by investigating the incidence of and reasons for end-of-life decisions in TTTS, which we termed 'intentional fetal or neonatal demise'. This study is described in *chapter 6*.

The sixth and final part of this thesis contains a summary followed by an overall discussion of the results of our studies into brain injury and neurodevelopment after TTTS in relation to the current medical literature. We will conclude the thesis by proposing future research directions in the field of TTTS. Despite significant progress made in recent decades, ongoing research efforts are essential to further improve the lives of affected families, such as Amy's and Rosie's, in the future.