A New Treatment Option for Fetal Aqueductal Stenosis: Ventriculo-Amniotic Shunt

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Statement of Purpose: Fetal aqueductal stenosis (AS) is a condition that affects 2-4 infants per 10,000 births. The condition leads to progressive hydrocephalus, with enlargement of the head necessitating delivery by cesarean section. Tearing of the nerve fibers distorted by the enlarging fluid spaces in the brain has sequelae of cerebral palsy, developmental delay, seizures, and diminished cognitive function. While this condition affects approximately 1,600-2,000 births per year in the United States, the societal costs are enormous on a broader basis. The stress on the family is far reaching, long lasting and can result in isolation and health issues for parents and siblings. The divorce rate is much higher for parents of special needs children. Present management for fetal hydrocephalus involves either preterm delivery followed by postnatal shunting or expectant management to term followed by shunting. Problems associated with early delivery are concomitant prematurity, poor surgical candidacy, and a greater rate of shunt complications. To address these issues, we developed a novel ventriculo-amniotic shunt using a composite tube, superelastic nitinol, and electrospun polyester membrane for treating fetal aqueductal stenosis.

Methods: Two commercially available catheters were used to fabricate prototypes. The 3Fr and 4Fr size tubes were obtained from Neuroform3® Microdelivery System (Boston Scientific, MA) and the Angiographic Catheter (SRD6913, Cordis, Johnson & Johnson Co., FL), respectively. Superelastic nitinol wires (Confluent, CA) were appropriately bent and went through the thermal shape setting process to fabricate anchors. The poly (ester-urethane-urea)s (PEUU) membrane was electrospun and attached on one end of the tube as the one-way valve to prevent backflow of the amniotic fluid to fetal brain. Both pressures and flow rates were measured by micro pressure sensors (Pendotech, NJ) and a liquid flow sensor (SLI-2000, Sensirion, CA). A load-cell equipped vertical translational stage (LSB200, Futek, CA) was used to quantify the nitinol anchor performance.

Results: The initial pressure in the fetal brain was set as 0.86psi and amniotic sac was 0.24psi. Therefore, the pressure difference between the two zones was 0.64psi (32mmHg). The fetal brain pressure ramped to as high as 4.2psi with the syringe pump running for 7.2s when the 7cm long shunt (4Fr catheter) was not connected into the system. The pressure elevation in fetal brain was found to be 388% and this high pressure represented the high risk of fetal brain damage. The pressure level in fetal brain first dropped to around 0.15psi and the pressure level in amniotic sac slightly increased to around 0.25psi once we turned on the valve. The pressure redistribution occurred between the fetal brain and amniotic sac and the excess cerebrospinal fluid drained from the brain to the amniotic sac. The corresponding flow rate in the shunt during this process was represented by the peak value, which was 4134.6uL/min. The ensuing flow rate was larger than the one in 3Fr case. Later on, the pressure level in fetal brain slowly increased to approximately 0.2psi with the syringe pump running for 7.2s. There was also a slight increase in the pressure level from 0.24psi to 0.29psi. Therefore, the pressure decrease in fetal brain was found to be 95.2% (from 4.2psi to 0.2psi) and the pressure elevation in amniotic sac was 20.8%.

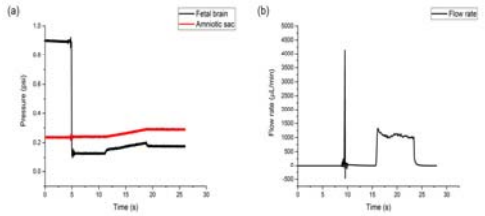

Figure 1. Pressure levels and flow rate in a 4Fr catheter shunt

Three prototype ventriculoamniotic shunts contain different anchor designs (Figure 2 (a)-(c)). The anchor dislodgement forces (i.e., resistance to the applied force) were quantified using a load cell, showing sufficient resistance as an anchor. Figure 2(d) shows the one-way valve used for the prototype. A qualitative test data demonstrated the functionality of the valve for controlling the flow in the shunt device. A PCT has been filed (Application No. PCT/US2016/056751) on October 13, 2016.

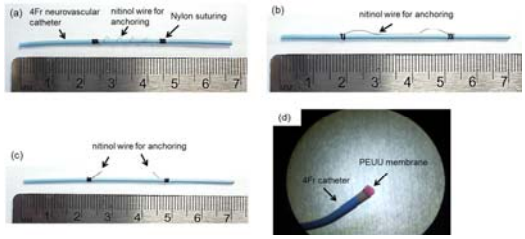

Figure 2 (a)-(c) three prototype devices with anchor designs, and (d) one-way valve at the end of the shunt device

Conclusions: A novel ventriculo-amniotic shunt prototype has been developed to treat fetal aqueductal stenosis. Findings from several *in vitro* laboratory studies have demonstrated the functionality of the device suggesting a new treatment option. *In vivo* animal tests are currently undergoing along with the prototype refinement. We estimate that US hospital costs saved is close to $80 million. The long term financial gains are more than $600 million to both healthcare facilities and families. We intend to speeding the availability of the humanitarian use device and its subsequent transition to market for this and other fetal applications. Our device would further aid in evolution of fetal neurosurgery as a novel medical speciality. Multiple research grants (>$100,000) have been funded including Center for Medical Innovation, McGowan Pediatric Device Initiative and Pitt Innovation Challenge at the University of Pittsburgh.

References: [1] Chen et al. Journal of medical engineering & technology. 2016, 40;186-198. [2] Emery et al. Fetal diagnosis and therapy, 2015,38:81-85. [3] Emery et al. Prenatal diagnosis, 2015, 35:319-324.