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## Technical aspects of laser surgery for TTTS

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# Chapter 5

Impact of Laser Power and Firing Angle on  
Coagulation Efficiency in Laser Treatment for  
Twin-Twin Transfusion Syndrome?  
An Ex-Vivo Placenta Study

# ABSTRACT

## Introduction

To assess the impact of laser power and firing angle on coagulation efficiency for closing placental anastomoses in the treatment of twin-twin transfusion syndrome (TTTS).

## Methods

We used an ex-vivo blood-perfused human placenta model to compare time to complete coagulation using 30W versus 50W of Nd:YAG laser power, and using a 90° versus a 45° firing angle. Placentas were perfused with pig blood at 5mL/min. Differences were analyzed using an independent samples T-test, Mann-Whitney U test and Chi-square test where appropriate.

## Results

Coagulation took less time and energy using 50W(n=53) compared to 30W(n=52); 11s vs. 22s,  $p<0.001$ , and 557J vs. 659J,  $p=0.007$ . Perpendicular coagulation (n=53) took less time and energy compared to a 45°-degree angle(n=21); 11s vs. 17s,  $p=0.004$  and 557J vs. 871J,  $p=0.004$ . Bleeding complicated 2(3%) measurements in the 50W group, 5(10%) in the 30W and 3(14%) in the 45° group.

## Discussion

In a highly controlled model, a 50W laser power setting was more energy efficient than 30W in coagulating a placental vein. A more perpendicular laser firing angle resulted in more efficient coagulation. Furthermore, bleeding due to vessel wall disruption occurred more often with lower power and a more tangential approach.

## INTRODUCTION

Fetoscopic laser surgery (FLS) is currently the best treatment modality for twin-twin transfusion syndrome (TTTS). De Lia et al. first proposed fetoscopic laser surgery in 1990.[1] In 2004 a randomized trial showed FLS to be superior to serial amnioreduction[2] and since then FLS has been widely adopted as the 'first-choice' treatment for TTTS.

Different types of laser and power settings have been used for this procedure. Most centers now use either a Neodymium-doped Yttrium Aluminum Garnet (Nd:YAG) laser with a 1064nm wavelength or a diode laser with a 940nm wavelength and power setting between 20 and 80 watts.[3] Both laser systems are continuously emitting laser systems with similar absorption properties. However, the optical penetration depth of the photons emitted by the diode laser is substantially lower than that of the Nd:YAG laser.[4]

In 2014 Slaghekke et al. showed that the Solomon technique, laser coagulation of the total vascular equator from one placenta margin to the other, was superior to the selective technique where only visible anastomoses are coagulated, in respect to recurrence of TTTS and incidence of post-laser twin-anemia-polycythemia sequence (TAPS).[5] With the Solomon technique, a larger surface area of the placenta is exposed to laser energy (time x power) and, in total, more energy is used during a procedure.

Laser firing angle is believed to be of importance for successful efficient coagulation.[6] The more perpendicular the laser fiber is pointed at the vessel, the faster coagulation is achieved. This is one of the reasons that choosing the optimal introduction site for the fetoscope is found to be one of the most important steps in the procedure.[7] However, the actual impact of a tangential approach has never been evaluated.

We hypothesized that faster, more efficient laser coagulation of placental vascular anastomoses would increase the safety and improve outcome in the treatment of TTTS. This study is a first step in proving this hypothesis, aiming to analyze the impact of laser power and firing angle on coagulation efficiency.

# METHODS

## Study design

This ex-vivo experimental human placenta study was conducted at the Department of Fetal Therapy of the Leiden University Medical Center between March 2015 and July 2015. After informed consent, term placentas from women with uncomplicated vaginal deliveries were obtained. Placentas were rinsed and stored at room temperature in a sodium chloride 0.9% solution directly after delivery. All experiments took place within 8 hours after delivery of the placenta.

Three groups of measurements were performed comparing laser power setting and laser firing angle. Group 1 consisted of measurements perpendicular to the vein with a power setting of 50 Watt. Group 2 consisted of measurement perpendicular to the vein with a 30-watt power setting and the third group of measurements was performed at a 45° angle to the vein with a 50-watt power setting. All placentas were randomly assigned to each group.

## Laser system

A Medilas Fibertom 5100 Nd:YAG laser (Dornier MedTech Europe GmbH, Weßling, Germany) with a 1064nm wavelength was used for all experiments. A 600µm bare-tip laser fiber was used which was replaced after every 25 measurements. The laser was serviced and calibrated before the study was started.

## Tissue preparation

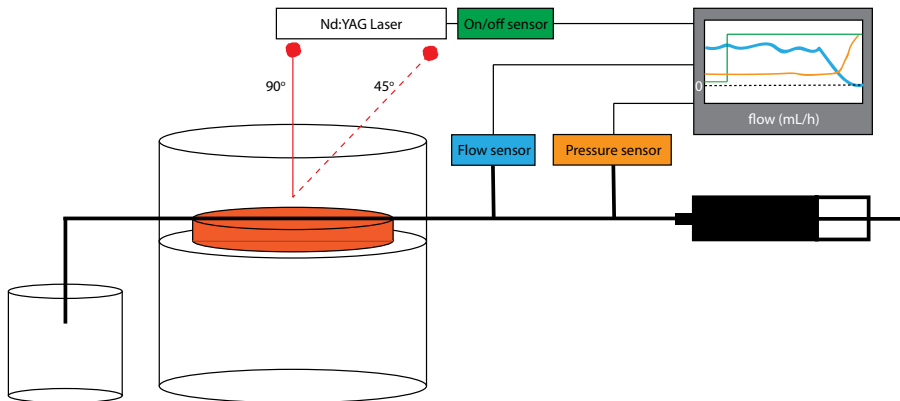
All placentas were screened for eligible veins with a diameter of approximately 1.5 - 2.0mm, relatively straight and without branches over a 2cm length. These vessels were dissected on both ends and cannulated with a 1.4mm plastic cannula. The cannulas were kept in place with a surgical stich. The placenta samples were casted in a 2% agar solution (Sigma-Aldrich Chemie B.V., Zwijndrecht, The Netherlands) filled 12cm petri dish with the maternal side downward with a layer of agar preventing the placenta to touch the bottom of the petri dish. The adhesive character of the agar solution prevented leakage from minor defects of the basal plate. A high-definition photograph was taken of each cannulated vessel. All vessel diameters were measured using ImageJ 1.47v software (ImageJ, National Institutes of Health, Bethesda, Maryland, USA).

## Experimental set-up

A diagram of the experimental set-up are shown in Figure 1. The placenta samples were

placed in a sodium chloride 0.9% bath, kept at a steady 37°C temperature. The cannulated vein was connected to the circulation system that consisted of a calibrated syringe pump (Fresenius-Kabi Pilot C, Zeist, The Netherlands) with  $\pm 2\%$  flow rate accuracy, connected to a P10EZ-1 pressure sensor (Becton Dickinson Medical, Franklin Lakes, USA) and a flow sensor (Transonic clamp-on 2pxl flow sensor with a Transonic TS410 amplifier). The laser fiber was kept in place by a system that allowed for easy and accurate adjustment, and was pointed either perpendicular or at a 45° angle at the vein. The distance between the laser fiber tip and the vein was kept at 4.0mm for each experiment.

Fresh heparinized (5.000 IU/L) pig blood with a 37°C temperature was used to circulate the placental vein. Flow rate was set at 5ml/min. The entire circulation was checked for leaks before each experiment.



**Figure 1** Diagram of the experimental set-up.

A computer program continuously measured the flow and the pressure in the circulation and the modulus of the laser system (on/off). Results of these measurements were plotted on a screen in real-time. Measurements started when the laser was activated and continued until successful coagulation of the vein was achieved. Successful coagulation was defined by a drop of the flow speed below 2.5mL/min without recovery. The noise on the flow sensor signal combined with the already low flow prevented us from using a flow of 0mL/min to define stagnation of flow. Time was automatically measured between activation of the laser and stagnation of flow. Concurrently, the total energy used in each experiment was calculated based on the power setting.

## Statistical analysis

Comparisons were made between group 1 and group 2, and between group 1 and group 3, with respect to time and energy used for successful coagulation defined as cessation of flow. Cases that were complicated by vessel wall disruption and bleeding were omitted from the analyses. Analyses were conducted using SPSS Statistics (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Normally distributed data were expressed as mean  $\pm$  standard deviation (SD) and compared using an independent samples T-test. Skewed data were expressed as median with range and were compared using a Mann-Whitney U test. For comparison of categorical data, a Chi-square test was used. A p-value of  $<0.05$  was considered statistically significant.

## RESULTS

Out of 37 fresh human placentas, a total of 126 viable samples were retrieved. A total of 126 measurements were conducted, successful coagulation was achieved in 116 samples. All results and comparisons between groups are shown in Table 1. Figure 2 shows a sample before and during successful coagulation.

### Group 1

In total 53 measurements were performed perpendicular to the vein with a 50 Watt laser power setting. In two samples (3%), bleeding occurred during coagulation of which in one case successful coagulation was achieved. 51 cases were eligible for analysis. Mean vessel diameter was 1.60 (SD 0.14) millimeter. Median time needed for cessation of flow in the vein was 11.1 seconds ranging from 1.4 to 32.8, which lead to a median energy used of 557 Joule ranging from 72 to 1639.

### Group 2

Fifty-two measurements were performed perpendicular to the vein at 30 Watt power. Five cases (10%) were complicated by bleeding and in two cases successful coagulation could not be achieved. 47 cases were analyzed. Mean vessel diameter in this group was 1.6 (SD 0.12) millimeter. Median coagulation time was 22.0 seconds ranging from 8.5 to 314.4. Median energy used for coagulation was 659 Joule and ranged from 254 to 9431.

### Group 3

At a 45° angle using 50 Watts laser power, 21 measurements were performed. Three samples (14%) were complicated by vessel wall disruption and in none of these successful

coagulation could be accomplished. Mean vessel diameter was 1.65 (SD 0.12) millimeter and median time for coagulation was 17.4 seconds ranging from 2.6 to 78.1 leading to a median total energy used of 871 Joule, ranging from 132 to 3906.

Coagulation took significantly less time and energy using 50W laser compared to 30W (11.1 vs. 21.0s,  $p < 0.001$  and 556 vs. 659 Joule,  $p = 0.007$ ). Perpendicular coagulation took significantly less time and energy compared to a 45°-degree angle (11.1s vs. 17.4s,  $p = 0.004$  and 556 vs. 871 Joule,  $p = 0.004$ ). Vessel diameter did not differ between 50W and 30W samples (1.6 vs. 1.6  $p = 0.347$ ) or between 90° and 45° samples (1.6 vs. 1.6mm  $p = 0.223$ ).

	Group 1 n=53 50 watt 90°	Group 2 n=52 30 watt 90°	Group 3 n=21 50 watt 45°	P-value 1 vs 2	P-value 1 vs 3
Laser duration (seconds)	11.13 (1.43 - 32.77)	21.98 (8.49 - 314.39)	17.42 (2.64 - 78.13)	<0.001*	0.004*
Laser energy used (Joule)	556.50 (71.50 - 1638.50)	659.40 (254.70 - 9431.70)	871.25 (132.00 - 3906.50)	0.007*	0.004*
Diameter of vein (mm)	1.61 ±0.14	1.63 ±0.12	1.65 ±0.12	0.347	0.223
Complications, bleeding	2 (3%)	5 (10%)	3 (14%)	0.116**	0.104**

**Table 1** Analysis of laser duration and total energy for each group. Values expressed as median (range), mean ±SD or as n(%). \* Mann-Whitney U test used. \*\* Chi-square test used. All cases where bleeding occurred were excluded in the analyses.

## DISCUSSION

This is the first study reporting on an ex-vivo perfused human placenta model to evaluate laser coagulation efficiency of different power settings for obliterating superficial placental vessels. To date, despite more than 25 years of laser surgery for TTTS, the ideal power setting for coagulation of anastomosis is unknown. Different strategies are being used, e.g. lower power setting at early gestational age at treatment or power setting dependent on size of the anastomosis.[3]

In this study we found that a higher power setting was associated with more efficient coagulation, shown by a shorter coagulation time and less energy used. In addition, we found that the firing angle significantly impacts the coagulation efficiency. A 45° angle almost doubles the amount of energy and time needed for successful coagulation compared to a perpendicular approach. With currently used equipment, optimization of

the angle of approach can only be achieved by careful selection of the site of entry of the fetoscope. Innovations in instrument design may be needed to optimize the efficiency of laser coagulation in difficult cases with anterior placenta or suboptimal position of the donor.

Bleeding due to vessel wall disruption, although rare, occurred slightly more often with lower power settings and with a more tangential laser angle. We hypothesize that a low power setting used for a longer period of time causes more endothelium damage[8] and without swift occlusion of the vessel by coagulated blood, this might increase the risk of vessel wall disruption and bleeding.

Recently, Zhao et al. showed that, after a laser procedure, more chorioamnionitis and funisitis is seen compared to non-lasered monochorionic (MC) twin pregnancies. [9] A possible explanation for this finding is the iatrogenic placental tissue necrosis caused by laser coagulation that may induce a maternal inflammatory response. In their study, a trend was seen towards more chorioamnionitis with higher energy use ( $p=0.06$ ). A previous study looked at the impact of laser coagulation on the ovine placenta with respect to local, collateral and peripheral damage at different time points after treatment.[10] This study showed that the tissue effect, especially collateral and peripheral, increases over time. Superficial vessel coagulation induced complete functional elimination of the involved cotyledon caused either by direct tissue damage and/or from arrest of cotyledonary flow, leading to ischemic necrosis. In this study, the impact of the amount of energy delivered and the relation to the tissue damage was not reported. A study evaluating different Nd:YAG power settings for the cutting and coagulation of pulmonary parenchyma with interstitial laser found that reducing the exposure time reduces local tissue coagulation even when the laser power output was increased.[11] Combining our results with previous research suggests that efficiency in the use of laser energy for laser treatment of TTTS might be beneficial and that a higher power setting and a perpendicular approach are more energy efficient, and safer, in attaining successful coagulation.

Although the highly realistic ex-vivo human placenta model we used eliminated many confounding factors, some limitations exist. The most important limitations of the model are the flow rate and the resistance of the circulation. It is difficult to accurately measure and control flow at flow rates below 5 milliliters per minute in a model. Not much is known about single anastomotic blood flow rates. Two studies reporting on anastomotic blood flow showed very different results, between 11.6mL/min with intra-amniotic Doppler measurements[12] and 5.6mL/24h based on calculation on decreasing hemoglobin levels

between intrauterine transfusion and birth[13]. The first one being highly unlikely due to the fact that the amount of flow exceeds the total blood volume of a mid-gestation fetus. Currently no reliable technique exists to assess single anastomotic blood flow. The higher flow rate used in this model, compared to true TTTS anastomotic flow, leads to longer coagulation time due to the heat sink phenomenon, constant dissipation of laser energy caused by blood flow from the coagulation site. Also, higher flow rate may result in higher pressure buildup during coagulation leading to a higher incidence of vessel wall disruption compared to in vivo coagulation of anastomoses in TTTS. Furthermore, the model uses pig blood instead of human blood, although this is similar to human in respect to size of red blood cells, red blood cell life span and hemoglobin content and structure.[14] These limitations cause that time and energy results may not exactly correspond to reality. However, the use of the model ensures that all measurements are performed under constant conditions. We do not expect that the limitations mentioned to have influenced the effect we showed. Future studies using the model will focus on using diode laser and multiple power settings to identify the optimal power setting for different types and size anastomoses.

## Conclusion

This study demonstrates that, in a highly controlled, though realistic, environment, a 50 Watt laser power setting is more efficient in coagulating a placental vein in respect to time and total energy needed compared to a 30 Watt laser power setting. In addition, we showed that the firing angle of the laser has a great impact on coagulation efficiency. The more perpendicular the approach the more efficient coagulation is achieved.

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