Acute Therapy Systems

Heart and Lung Assist for Pediatric Patients

novalung | medos

FRESENIUS MEDICAL CARE

Xenios, a Fresenius Medical Care Company, is a pioneer in the field of extracorporeal heart and lung support – for new dimensions in patient well-being. In contrast to standard therapies in this field, patients can remain awake, mobile, and self-determined[1] with our extracorporeal therapies. They may then spend less time in the intensive care unit[2], which helps to improve their prognosis of treatment[3].

Our therapies for pediatric patients are focused exclusively on the pediatric and neonatal fields, and answer the specific need with a broad product portfolio for the full spectrum of extracorporeal pulmonary and cardiac support. Products can be tailored to each child patient's individual needs[4].

This specific novalung and medos product portfolio directly addresses the particular challenges associated with the treatment of this young and diverse group of patients.

- **Challenge 1:**
  Different types of patients – from neonates up to young adults
- **Challenge 2:**
  Opportunity to use extracorporeal support as long as needed
- **Challenge 3:**
  Special demands for neonatal patients
- **Challenge 4:**
  Special patient group – reacting more sensitive to any change in setting, therapy or parameter

Challenge 1: Different Types of Patients – From Neonates up to Young Adults

Requirement

- Membrane lungs for a broad range of blood flow
- Huge variety of patient kits with different connector size, pump disposables and lengths for pediatric patients
- Target blood flow range to be covered for all pediatric patients

Solution

- Different patient kits: Wide range of preconfigured kits, tailored to the needs of the pediatric patient population
- Xenios console as one platform and pump (DP3) offer the full range of support

Reference

“ The low priming volume (16 mL), wide range of flow rate (0–8 L/min), rotation speed (0–10,000 rpm), and production of pressures up to 600 mm Hg allow it to be used in both pediatric and adult patients”[5)]

“ increased flow range offers a higher level of flexibility and safety for a wide range of applications”[5)]

“ In conclusion, the DP3 can be used for individual patient demands and adapted to their most suitable method of support. Meticulous flow adjustments render this pump highly effective for extracorporeal support particularly in pediatric patients.”[4)]

Challenge 2: Opportunity to Use Extracorporeal Support as Long as Needed

Requirement

- Long-term approved patient kits

Solution

- Novalung patient kits certified for 29 days application period

Reference

“ We used the same ECLS system for up to two weeks without changing it” [6]

“ […] enabled intensive care specialists to use VV-ECMO not only as a short-term rescue procedure, but also as a long-term application and bridge to transplantation in adult as well as pediatric patients.” [7]

“ Within the development and introduction of long-running ECMO devices (including heparin coated tubing, special microfiber polymethylpentene membranes, rotating blood pumps, and percutaneous catheters) with week-long stability […]” [8]

Challenge 3: Special Demands for Neonatal Patients

Requirement

- Sensitive flow adjustments at low flow ranges with less turbulences and reduced hemodilution

Solution

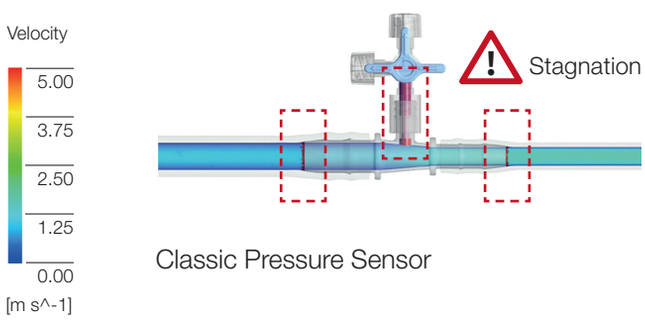
- DP3 pump allows flow adjustment in steps of 10 ml/min (requires ¼" patient kit and ¼" flow sensor)
- Reduced turbulence because of continuous tubing diameter
- Integrated Pressure Sensor (IPS) attributed for less hemodilution, reduced risk of air aspiration and clotting in pediatric patient

Reference

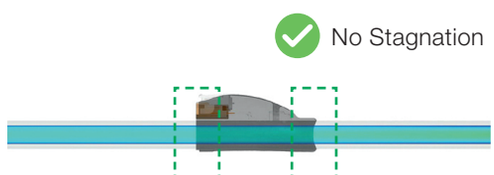
“ It was shown that calculated low flow rates needed for support particularly in neonates can be maintained over a long period of time.” [9)]

“ Critical elements of construction related to the whole system are the connecting tubes, which conically increase from the venous ¼ inch to 3/8 inch at the pump entrance. This may predispose to turbulent flow and thrombus formation.” [9)]

Connector Fluency Chart



Classic Pressure Sensor



Integrated Pressure Sensor (IPS) with continuous tubing diameter

Challenge 4: Special Patient Group – Reacting More Sensitive to Any Change in Setting, Therapy or Parameter

Requirement

- Safety features for more secure extracorporeal treatment of pediatric patients

Solution

- Xenios console provides several safety features for example bubble detection
- One platform and pump (DP3) offer the full range of support
- Possiblility to connect a heater cooler unit to the circuit for temperature management

Reference

“ Safety functions are ensured by several control systems: cannula aspiration is prevented by preload control; a brief interruption of the flow can be managed with the zeroflow mode without risking backflow.” [10)]

“ […] it is the prevention of backflow and features for pressure, bubble and flow control offering fine adjustments down to zero, which make the DP3 safe.” [9)]

“ The system was complemented with an MDC console, which included valuable safety mechanisms such as a flow sensor with an integrated bubble detector, backflow detection, and temperature sensors.” [5)]

By Your Side

Clinical Support

We accompany excellent use of our technology and implementation of our therapies with far-reaching individual support and application-oriented services. This includes an international support hotline.

Our console is always accompanied by comprehensive support from our Clinical Support Team. Each of our application specialists has many years of real-world experience from specialists working in clinics. These highly qualified experts provide with on-site support – comprising instructions/training and help in implementing our technology in the day-to-day business of your clinic.

Technical Service

Our Technical Service Team is available to answer any and all technical questions you may have in and around the Xenios platform. In addition to this, the Academy offers you professional events for both basic and advanced training. The Xenios campus- our e-learning platform - offers divers study modules and videos tailored to your specific areas of interest.

References

1 Langer et al., (2016) "Awake" extracorporeal membraneoxygenation (ECMO) : pathophyiology, technical considerations, and clinical pioneering. Critical Care 20:150.

2 Braune S. et al. (2015) The use of extracorporeal carbon dioxide removal to avoid intubation in patients failing non-invasive ventilation--a cost analysis. BMC Anesthesiol 15:160.

3 Teno JM et al., (2000) Decision - Making and outcomes of Prolonged ICU Stays in Seriously Ill Patients. J Geriatr Soc.; 48 (5 Suppl): 70-4.

4 Speth, Marlene et al. (2016) Pediatric extracorporeal life support using a third generation diagonal pump. ASAIO J. 62(4):482-490: 482.

5 Okan, Yildiz et al. (2017) Initial Clinical Experiences With Novel Diagonal ECLS System in Pediatric Cardiac Patients. Artifical Organs 41(8):717-726: 718.

6 Okan, Yildiz et al. (2017) Initial Clinical Experiences With Novel Diagonal ECLS System in Pediatric Cardiac Patients. Artifical Organs 41(8):717-726: 722.

7 Schmidt, Florian et al. (2012) Concept of “awake veno-venous extracorporeal membrane oxygenation” in pediatric patients awaiting lung transplantation. Pediatric Transplantation: 1.

8 Schmidt, Florian et al. (2012) Concept of “awake veno-venous extracorporeal membrane oxygenation” in pediatric patients awaiting lung transplantation. Pediatric Transplantation: 5.

9 Speth, Marlene et al. (2016) Pediatric extracorporeal life support using a third generation diagonal pump. ASAIO J. 62(4):482-490: 489.

10 Stiller, Brigitte et al (2017) Multicenter Experience With Mechanical Circulatory Support Using a New Diagonal Pump in 233 Children. Artficial Organs: 3.

FRESENIUS
MEDICAL CARE

End of 2016, Xenios became a part of Fresenius Medical Care, the world’s leading provider of products and services for people with chronic kidney failure.

Head office: Fresenius Medical Care Deutschland GmbH · 61346 Bad Homburg · Germany
Phone: +49 (0) 6172-609-0 · Fax: +49 (0) 6172-609-2191

www.freseniusmedicalcare.com

Mechanical extracorporeal circulatory support in pediatric patients

using a third-generation diagonal pump

THIS SUMMARY INCLUDES THE FOLLOWING STUDIES:

- Stiller et al.: European, multicenter, retrospective cohort study with 233 pediatric patients investigating efficacy and safety of Deltastream DP3 for respiratory and cardiopulmonary support [1]
- Speth et al.: Single-center study on experiences with the use of Deltastream DP3 for cardiac, pulmonary, or combined support in 27 pediatric patients [2]
- Fleck et al.: Retrospective, serial analysis of 16 children investigating feasibility and safety of Deltastream DP3 in pediatric patients with post-cardiotomy heart failure, cardiopulmonary resuscitation, or acute respiratory distress syndrome [3]
- Barbaro et al.: International report of the Pediatric Extracorporeal Life Support Organization (ELSO) Registry describing the growth, outcome, complications, and technologies of pediatric extracorporeal life support from 2009 to 2015. Until today, 59,969 children are listed in the registry [4]

BACKGROUND

For many years extracorporeal life support (ECLS) has been saving the lives of children with acute or reversible cardiopulmonary failure. Using veno-venous (v-v) or veno-arterial (v-a) extracorporeal membrane oxygenation (ECMO), circulatory and respiratory function can be restored in patients protecting them from irreversible organ damage. Moreover, time to recovery or transplantation may be bridged and used for therapies or decision making [1].

ECMO treatment worldwide continues to be regularly performed using traditional roller pumps or first-generation centrifugal pumps, but survival and long-term outcomes of patients might be compromised by system-related complications (e. g. hemolyse, thromboembolic events, systemic inflammation). Such complications cannot be entirely prevented, but technical innovations might reduce them by improving flow characteristics of extracorporeal circuits (box 1) [1-3].

The Deltastream DP3 (Medos, Medizintechnik AG, Stolberg, Germany) is a diagonal pump (centrifugal pump) allowing a huge variation of blood flows. The reduced size of the extracorporeal circuit enables uncomplicated transport as well as rapid set-up and is easier to handle in ECLS-based resuscitation in case of circulatory arrest as compared to traditional systems [2].

Below, the Deltastream DP3, which is used in Europe for neonatal and pediatric patients, is introduced in detail. Furthermore, efficacy, complication, and survival rates associated with the new generation diagonal pump are evaluated.

THE DELTASTREAM DP3 DIAGONAL PUMP

The Deltastream DP3 (Medos, Medizintechnik AG) is a diagonal pump with a diagonally streamed impeller (fig. 1 A, B), which combines the advantages of radial and axial pumps: high hydraulic performance of radial pumps and small size plus low inertia* of axial pumps (fig. 1 C).

Because of the flexible position options the pump can be operated with shortened tube lengths, thus minimizing the priming volume and blood contact with foreign surfaces. The pump system itself requires a priming volume of 16 mL only. The Deltastream DP3 generates a flow of

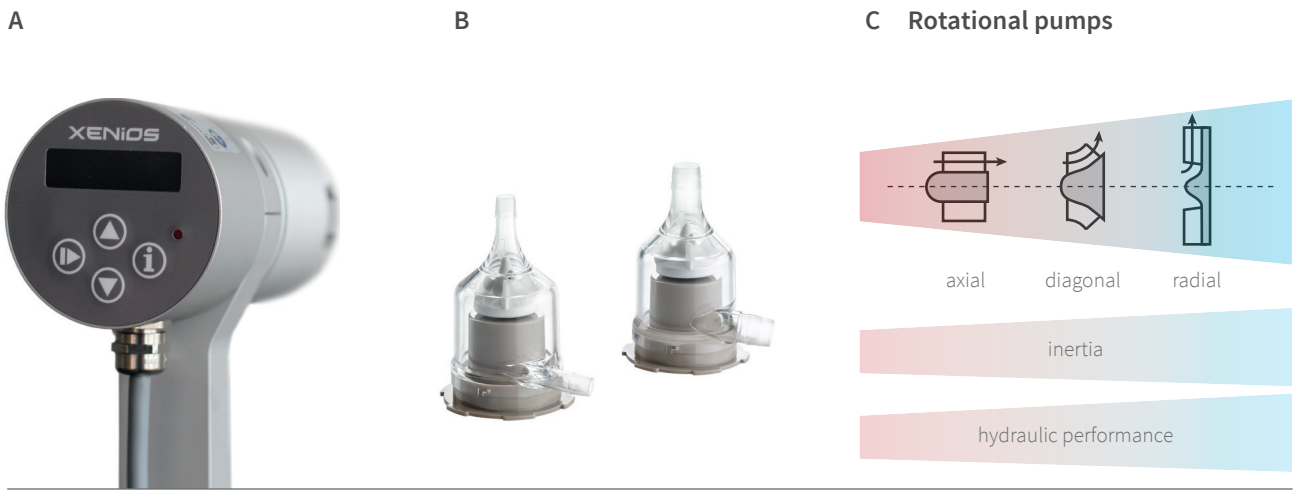


Figure 1. **A** Photo of the DP3 console (Xenios AG). **B** Photo of the Deltastream DP3 pump heads (Medos Medizintechnik AG): 1/4"-connection (left) and 3/8"-connection (right). Owing to a ring magnet and a ceramic ball-bearing, the impeller is pivoted and associated with low friction loss. Due to the novel impeller design, the DP3 does not require a seal to prevent leakage. **C** The DP3 is a centrifugal pump with a diagonally streamed impeller and combines the advantages of radial pumps (high hydraulic capacity) with the small size and low inertia of axial pumps; modified according to [1].

* The resistance to react or interact with other substances/materials

up to 8,000 mL/min and a pressure of ≤ 600 mmHg at a maximum rotational speed of 10,000 revolutions per minute. Blood flow can be adjusted to individual needs even below 0.5 L/min which enables the application on patients of every age. **Several control systems guarantee its safety.** The P1-limiter (preload control) prevents cannula aspiration, and a zero-flow mode allows brief interruption of the flow without risking backflow in the extracorporeal system. The Deltastream DP3 is applicable in all areas of mechanical circulatory support (v-v and v-a ECMO, ECLS or as ventricular assist device [VAD]), and due to its design it is associated with a reduced risk of cavitation bubbles and extreme negative pressures as compared to roller pumps [1-3].

Box 1: Statements on safety of the Deltastream DP3 system in studies.

Study	Statements on safety of the DP3
Stiller et al. 2017 [1]	• Multicenter study with 233 children suffering life-threatening cardiorespiratory failure: - the DP3 is highly effective with a high weaning rate of 73 % and a very good survival rate until discharge of 59 % - successful application of the DP3 in pediatric patients with large range of diagnoses, ages, and bodyweights • Blood flow of the DP3 adjustable, even below 0.5 L/min: - allows application of the DP3 in neonates to adults • Safety of the DP3 improved by different control functions: - P1-limiter of the DP3 (preload control) prevents cannula aspiration - zero-flow mode of the DP3 allows brief interruption of the flow without backflow in the extracorporeal system • Applicability of the DP3: - v-v ECMO in patients with pulmonary failure and v-a ECMO in patients with combined cardiopulmonary failure - as ventricular assist device (VAD) in patients with cardiac failure and preserved lung function • Recommended to have a pre-connected DP3 set at hand with short tubes and a small priming volume: - to ensure rapid preparation of the pump - to stabilize circulation and respiration of pediatric patients as quick as possible – inside and outside the hospital
Speth et al. 2016 [2]	• Calculated low flow rates (especially necessary for neonates): - can be maintained over long periods of time by the DP3 • Important safety features of the DP3: - prevention of backflow - control functions regarding pressure, bubbles, and blood flow with the possibility of fine adjustments of blood flow down to zero • Owing to reduced shear stress from the bearing of the DP3: - prevention of heat generation of the pump (more gentle treatment of blood components as compared to previous systems) • In the heterogenic pediatric study population: - the DP3 is a multifunctional system for mechanical circulatory support - adaptation of the DP3 to individual circumstances and needs of the patient – also in low flow range – is possible • Through fine adjustments of blood flow: - DP3 is highly effective especially for extracorporeal support of pediatric patients
Fleck et al. 2013 [3]	• DP3 with diagonally streamed impeller: - combines good hydraulic properties of radial pumps with small size and inertia of axial pumps - enables blood flow of ≤ 8,000 mL/min and pressure of ≤ 600 mmHg - needed priming volume of the pump system itself only 16 mL • DP3 operable because of flexible position options with shortened tube lengths: - reduction of priming volume - minimization of blood contact with foreign surfaces

STUDIES WITH DELTASTREAM DP3 – DATA RELATING TO EFFICACY, COMPLICATIONS, AND SURVIVAL RATES

In a large retrospective cohort study with 233 pediatric patients (median age: 1.9 years [0–201 months]) in seven European centers the application of a Xenios system (Medos Deltastream console or iLA activve console) was analyzed. Patients with severe conditions and bad survival prognosis were included. Cardiopulmonary support via v-a ECMO was applied in 162 patients, respiratory support via v-v ECMO in 63 patients and application as ventricular assist device (VAD) was performed in eight patients** [1]. Mean duration of application was 5.5 (0.2–69) days and the

** Indication for use of the DP3 was either of cardiac origin (weaning failure from cardiopulmonary bypass, low cardiac output syndrome [LCOS] after cardiac surgery, chronic cardiac disease [e. g. cardiomyopathy or myocarditis] or cardiac arrest with extracorporeal cardiopulmonary resuscitation [E-CPR]) or of primary pulmonary origin (acute respiratory distress syndrome, pneumonia, lung hypoplasia in congenital diaphragmatic hernia or meconium aspiration syndrome).

weaning rate was 73 %. In total, 59 % of patients (pulmonary group: 62 %, cardiac group: 55 %) were discharged home and the complication rate was comparatively low (tab. 1). Complications mainly included bleeding, kidney function, and cerebral thromboembolism as well as sepsis. **Only 2 % of complications were due to technical failure** (tab. 1). An extracorporeal cardiopulmonary resuscitation was necessary in 24 patients whose survival-to-discharge rate was 38 %.

Table 1: Complications in 225 patients treated with Deltastream DP3.

Complications	n	%
None	106	47
Bleeding	75	33
Renal support	64	28
Cerebral thromboembolism	23	9.9
Seizures	3	1.3
Sepsis (blood-culture positive)	21	9.0
Others	10	4
Technical failure	5	2

Data of n = 8 patients is missing. Multiple answers possible [1].

The multivariate analysis showed effects on therapy outcome (death on device or death before discharge) upon exchange of the support system, complications, and renal support. For example, the death-on-device rate was 56 % in patients who switched the support system as compared to 36 % in patients without exchange (Odds Ratio [OR]: 1.94 [1.00–3.75], p = 0.049). Patients with complications had a death-before-discharge rate of 54 % versus 30 % in patients without complications (OR: 2.56 [1.43–4.60], p = 0.002). Patients with renal support*** exhibited a rate of 66 % in contrast to 31 % in patients without renal support (OR: 3.43 [1.80–6.53], p = 0.0002) [1].

Another study concludes that the Deltastream DP3 pump is a multifunctional device for mechanical support, which can be adapted to the individual circumstances and needs of patients – even in low flow ranges [2]. An extracorporeal cardiac, pulmonary, or combined support using Deltastream DP3 was performed in a pediatric cohort of 27 patients (median age: 278 days [0 days–14.2 years], median bodyweight: 7.2 kg [2.5–39 kg], median duration of support: 8 days [2–69 days]). Flow rates for neonates (n = 8) were between 0.2 L/min and 0.75 L/min. An irreversible pump damage occurred in one patient during de-airing after air block in the pump head. Weaning rate, 30-day-survival and hospital survival rate were 89 % (n = 25), 86 % (n = 24), and 71 % (n = 20), respectively [2].

Also Fleck and colleagues investigated the Deltastream DP3 in a small pediatric cohort (N = 16). In total, 75 % of patients (n = 12; 16 cases respectively [71 %]) were weaned successfully and 50 % of patients were discharged home after having received mechanical circulatory support for four days on average (0–18 days). **No system-related complications occurred, and none of the patients experienced severe bleeding or relevant thromboembolic events during treatment** [3].

DISCUSSION

The DP3 was successfully applied to patients of a large cohort study with a multiplicity of diagnoses and a large range of ages and bodyweights. **The novel third-generation diagonal pump proved to be highly effective with a high weaning rate (73 %) and very good survival-to-discharge-home rate of 59 %** [1]. This is comparable to the discharge rate of the ELSO Registry from 2017 (61 %) [4].

The study demonstrated that the DP3 is not only suitable for v-v ECMO in children with respiratory failure or v-a ECMO in children with cardiac failure, but also as ventricular assist device (VAD) in patients with cardiac failure and preserved lung function [1]. **Furthermore, it is advisable to have a pre-connected set with short tubes and small priming volume at hand to ensure rapid preparation of the pump. Thereby, the circulation and**

*** Decision for renal support was independent of ECMO application

respiration of children can be stabilized as quickly as possible – inside and outside the hospital [1].

The study of Speth and colleagues showed that the calculated low flow rates needed especially for the support of neonates can be maintained over long periods of time. In addition, safety features of the Deltastream DP3 such as prevention of backflow and control functions regarding pressure, bubbles, and flow provide important advantages. Fine adjustment of blood flow is possible in 10 mL-steps or by 50 rotations per minute down to zero. Also, heat generation by the pump is avoided due to reduced shear stress from the bearing leading to a more gentle treatment of blood components than in previous systems [2]. The DP3 is connected to a console (MDC, Medos Medizintechnik AG), which contains a bubble sensor as well as four pressure sensors to control blood flow and pressure within the system [2].

Also Fleck and colleagues affirmed that the Deltastream DP3 pump is effective for mechanical circulatory support in children and seems to cause only mild hemolysis. That is why the group has since been using the DP3 system as the standard blood pump for mechanical circulatory support in neonates and children [3].

In the study, the overall survival rate was 50 % (n = 8), which is lower than in the ELSO Registry (61 %). Yet, the proportion of 52 % cardiac indications (cardiac plus cardiopulmonary indications) was smaller than in the study of Fleck and colleagues (81 %) [3, 4]. However, the differences in survival rates could also be related to the very small patient population in the study of Fleck and colleagues limiting its statistical power.

CONCLUSION

In the last few years, a trend can be seen turning away from traditional roller pumps towards miniaturized centrifugal pumps. **The third-generation diagonal pump, Deltastream DP3, convinces by its easy handling, the multifunctional applicability, and its efficacy with very good survival and low complication rates.** The versatile pump can be adapted to individual patient needs, even if low flow rates are required. The DP3 enables E-CPR as well as patient transport with continued treatment in all age groups. Therefore, the highly mobile pump system is not only applicable in the operating room or intensive care unit, but also in other areas inside and outside the hospital allowing the stabilization of children's circulation and respiration as quick as possible. Furthermore, stable transport of patients with respiratory failure is easier with a mobile ECMO system than using high-frequency oscillation ventilation.

LITERATUR

[1] Stiller B, Houmes RJ, Ruffer A, et al. Multicenter experience with mechanical circulatory support using a new diagonal pump in 233 children. Artif Organs 2018;42(4):377-85

[2] Speth M, Munch F, Purbojo A, et al. Pediatric extracorporeal life support using a third generation diagonal pump. ASAIO J 2016;62(4):482-90

[3] Fleck T, Benk C, Klemm R, et al. First serial in vivo results of mechanical circulatory support in children with a new diagonal pump. Eur J Cardiothorac Surg 2013;44(5):828-35

[4] Barbaro RP, Paden ML, Guner YS, et al. Pediatric extracorporeal life support organization registry international report 2016. ASAIO J 2017;63(4):456-63

XENIOS AG

Im Zukunftspark 1
74076 Heilbronn
Germany

info@xenios-ag.com
www.xenios-campus.com
www.xenios-ag.com