



**FRESENIUS
MEDICAL CARE**

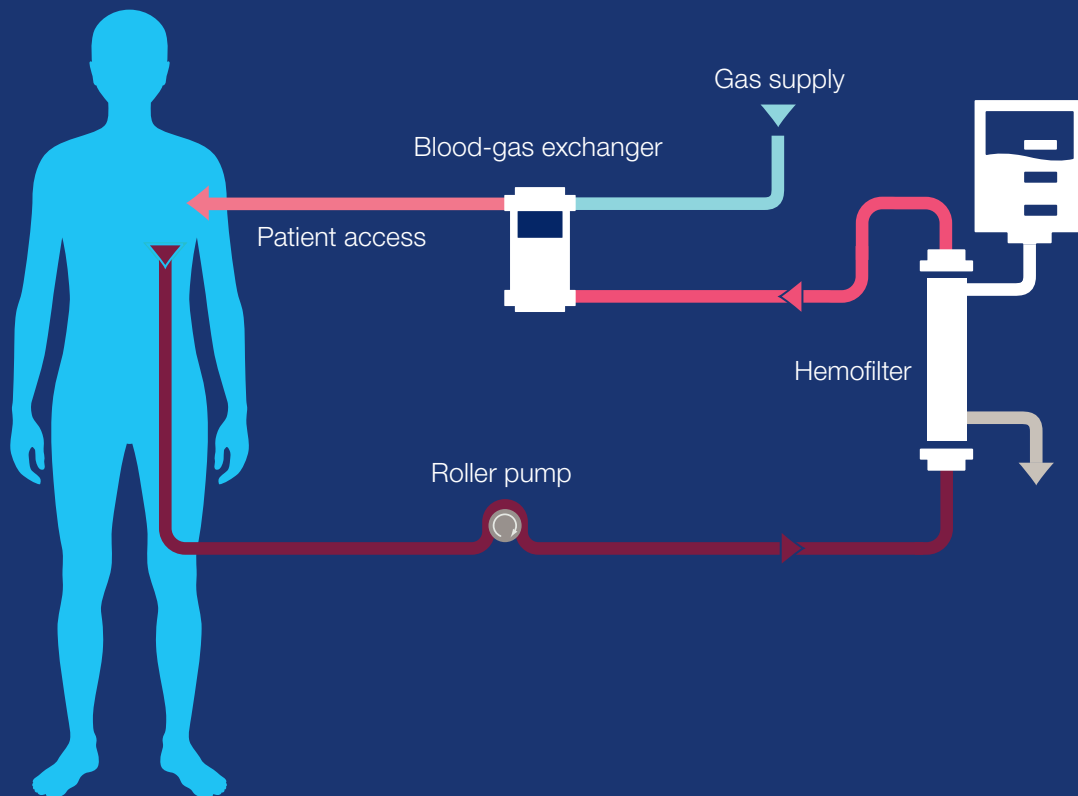
Acute Blood Purification



multiECCO2R

**Extracorporeal, partial CO₂ removal
in patients with compromised lung function**

General overview of ECCO₂R



Low-flow ECCO₂R in combination with CKRT

Characteristics

Extracorporeal carbon dioxide removal (ECCO₂R) to treat hypercapnia and respiratory acidosis:¹

- Used for blood decarboxylation, not for blood oxygenation¹
- Compared to extracorporeal membrane oxygenation (ECMO), blood flow can be lower because most CO₂ in the blood is not bound to hemoglobin (in contrast to O₂) but is transported in blood mainly as bicarbonate. In addition, CO₂ diffuses more readily across a gas exchange membrane due to better solubility.²
- CO₂ is eliminated via a hollow fiber gas exchange membrane. O₂ or medical air is used as sweep gas.¹

ECCO₂R techniques

Technique	ECCO ₂ R		ECMO
	– Low-flow – CKRT-based or stand-alone	Mid-flow	High-flow
Clinical indications	– Hypercapnia and/or respiratory acidosis during ARDS³ – Acute exacerbated COPD with imminent invasive ventilation³ – Reduction of lung stress⁴		– Acute refractory hypoxemia⁴ – Acute infectious respiratory failure⁵
Blood flow in studies (ml/min)	200 to < 500 ml/min ^{6,7-11}	500–1,500 ml/min ^{8,12-15}	> 1,500–7,000 ml/min ^{5,13}
Sweep gas flow in studies (l/min)	6–10 l/min ^{6,7,9,16,17}		
Catheter/cannula	Double-lumen catheter, 13.5–15.5 Fr ^{6,8,9,11}	Double-lumen cannula or two separate cannulas, 18–24 Fr ^{8,14}	2–3 separate cannulas, 21–31 Fr ⁵
Connections	VV ¹	VV, AV ¹	VA ¹⁶ , VV ⁵
CO ₂ removal (% baseline)	20–42% ^{11,13,18}	50–60% ¹⁹	> 50% ²⁰
Priming volume (ml)	140–320 ml ^{1,19}		300–750 ml ^{5,1}
Anticoagulation	Citrate (currently only available for use with multiECCO2R), heparin	Heparin	Heparin
Membrane surface area (m ²)	0.32–1.81 m ² ^{1,21,22}	0.65–1.3 m ² ^{1,20}	1.8 m ² ²⁰

Overview of parameters mentioned in the literature for ECCO₂R and ECMO techniques. There are no commonly agreed definitions to distinguish between ECCO₂R with low- and mid-flow.

CKRT = continuous kidney replacement therapy, ECCO₂R = extracorporeal carbon dioxide removal, ECMO = extracorporeal membrane oxygenation, VV = venovenous, VA = venoarterial, AV = arteriovenous

Clinical applications of ECCO₂R

Hypercapnia in patients with ARDS increases clinical risk

- Acute hypercapnia ($\text{PaCO}_2 \geq 50$ mmHg) is an independent risk factor for increased mortality in patients with ARDS²³⁻²⁵
- Acute hypercapnia is associated with higher rates of complications, organ failure and mortality²³

Hypercapnia can become an issue in ARDS patients with lung-protective ventilation

- Hypercapnia is a common reason for withholding lung-protective ventilation^{16,26}
- Ultra-protective ventilation with $V_T < 6$ ml/kg BW may require extracorporeal CO₂ removal²⁷
- Experts consider hypercapnic respiratory acidosis in patients with AKI as a relevant indication for ECCO₂R²⁸
- A multi-center trial in 51 ICUs naïve to the intervention aimed to lower tidal volume facilitated by low-flow ECCO₂R during heparin anticoagulation. It did not find any effect on 90-day mortality, but did report an increased risk for intracranial hemorrhage.²⁹

First clinical results indicate positive effects of ECCO₂R in ARDS patients*

- May counteract respiratory acidosis during lung-protective ventilation^{7,10,30,31}
- Enabled ultra-protective ventilation in hemodynamically unstable patients with a reduced need for vasopressors^{7,11,32}

* Study evidence is currently (09/2022) based on unblinded case series with diverse ECCO₂R techniques

Hypercapnia increases the risk of intubation for patients with aeCOPD

- Hypercapnia in patients with COPD is associated with increased incidence of hypoxia³³
- A significant proportion of patients with aeCOPD and non-invasive ventilation (NIV) requires intubation, which increases mortality risk⁴

Exploratory studies have investigated the integration of ECCO₂R into treatment strategies for aeCOPD*

- Supports non-invasive ventilation in patients with aeCOPD³⁴⁻³⁶
- In patients with imminent failure of NIV, it may be more cost-efficient than switching to invasive ventilation¹²

Important decision criteria for initiation of ECCO₂R when NIV failure is imminent

Results of an expert consensus⁴

Parameters	Expert consensus
No decrease in PaCO ₂ while on NIV	≥ 80%
No decrease in respiratory rate while on NIV	≥ 80%
Clinical signs of respiratory failure	≥ 50%
pH 7.25–7.30	≥ 50%

Specifications of multiECCO2R with multiFiltratePRO

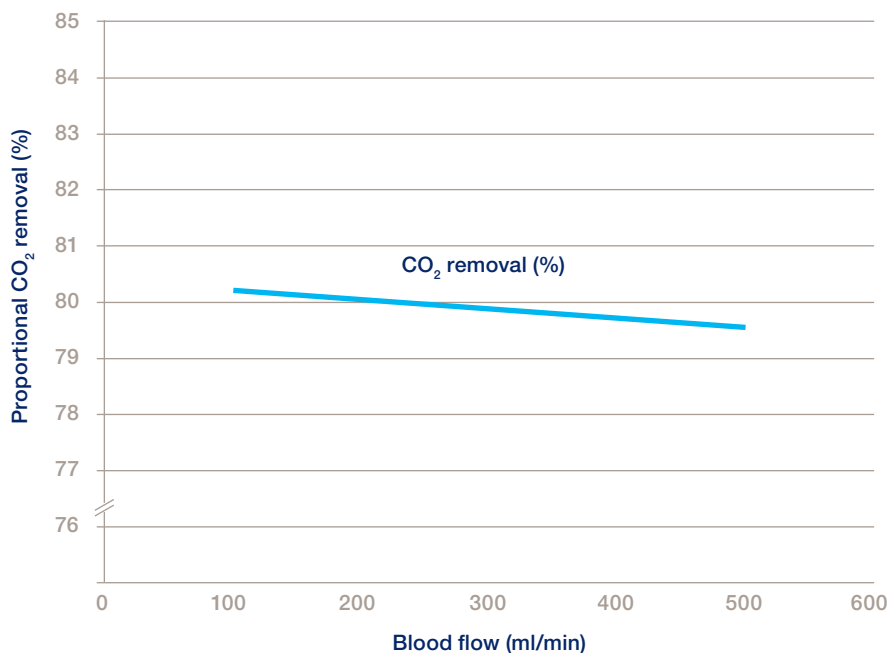
Low-flow ECCO₂R with multiECCO2R

Configuration: In combination with CKRT with multiFiltratePRO or multiFiltrate

Therapeutic objective: Partial CO₂ removal from patient blood for the treatment of hypercapnia in adult patients

- Provided effective treatment of hypercapnia in first pilot study (n = 4)⁶
- Does not require an additional vascular access due to its integration into the dialysis circuit²¹
- May be handled by nursing staff, no perfusionist support required³⁷
- Anticoagulation with citrate or heparin
- Maximum usage time: up to 72 h²¹

Consistent, efficient CO₂ removal with blood flow from 100 to 500 ml/min



Percentage of CO₂ removal at 72 h under standardized laboratory conditions

Gas/blood flow ratio 15:1, blood conditions at device inlet 37°C, CO₂ partial pressure (pCO₂) 95 mmHg, pH 7.15, venous saturation (vSat) 70%²¹

Clinical experiences with multiECCO2R

Case series with COVID-19 patients⁶

Patients: mild-to-moderate ARDS with refractory hypercapnia ($\text{PaCO}_2 > 55 \text{ mmHg}$). Two patients with COPD, three with CKD, BMI 24.3–42.1

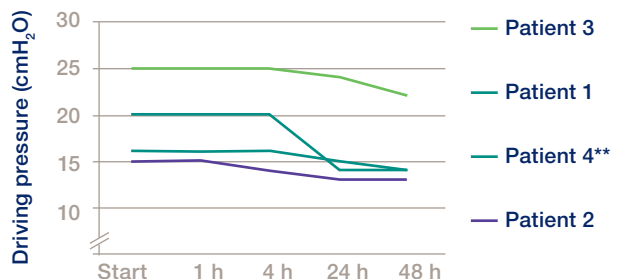
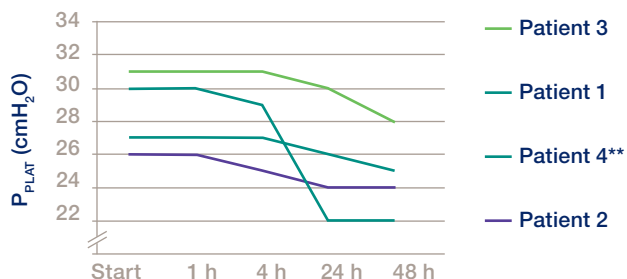
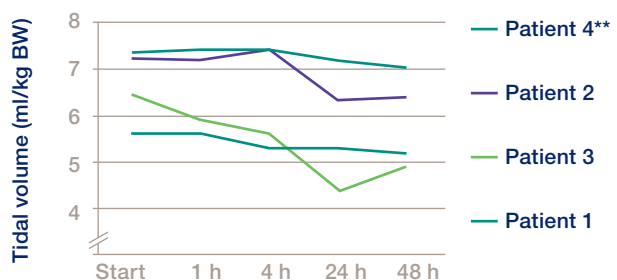
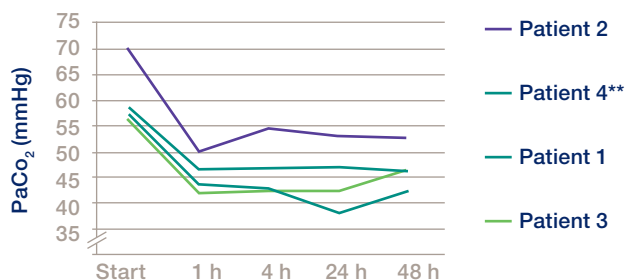
Ventilation: V_T 5.6–7.3 ml/kg, PEEP 6–11, prone positioning, three patients receiving supplemental nitrous oxide

Treatment goal: lung-protective ventilation

Settings: multiECCO2R on multiFiltrate devices in stand-alone or CVVHD mode, cannula 13.5 Fr, gas/blood flow ratio 15:1, external blood warmer

multiECCO2R stand-alone: blood flow 400 ml/min, gas flow 6 l/min, anticoagulation with heparin and aPPT target 60–80 s

multiECCO2R with CKRT: blood flow 200 ml/min, gas flow 3.5 l/min, anticoagulation with citrate



**Patient on ECCO₂R and CKRT with citrate anticoagulation

Development of selected ventilation parameters during the first 48 h in four patients with ARDS and COVID-19. Driving pressure = Plateau pressure – PEEP, PaCO_2 = Carbon dioxide partial pressure, P_{PLAT} = Plateau pressure

“In all four patients, the ECCO₂R treatment could be terminated after a median of 5.5 (4.5–7.5) days due to a sustained improvement in hypercapnia.”⁶

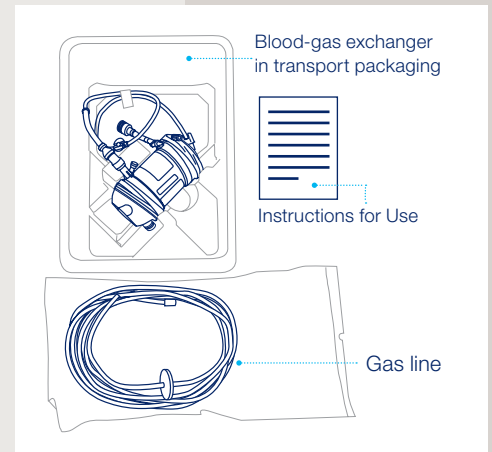
“Importantly, these data also implicate that every ICU with available dialysis may apply RRT platform-driven ECCO₂R to limit ventilator-induced lung injury or rescue uncontrollable respiratory acidosis even in situations where ‘standard’ ECCO₂R consoles are not available.”⁶

How does multiECCO2R work on multiFiltratePRO?

Setup

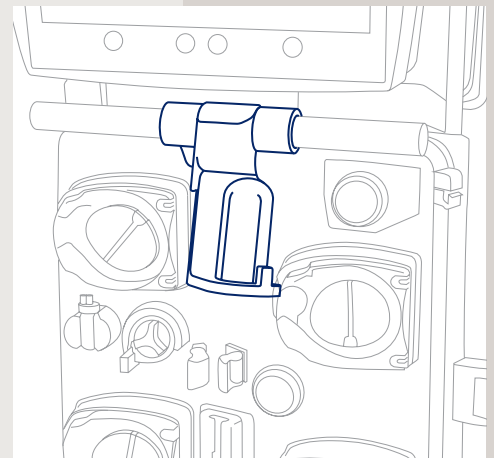
After opening the delivery set of the multiECCO2R, the following parts are available: blood-gas exchanger, sweep gas line, instructions for use.

It is assumed that the cassette for continuous kidney replacement therapy (CKRT) has been set up in advance.



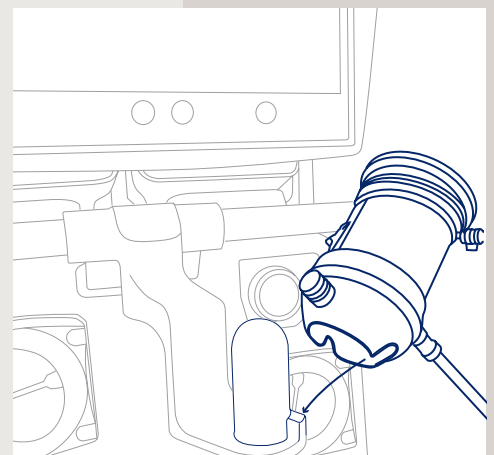
Step 1

The holder for the multiECCO2R is positioned in the middle of the front handle.



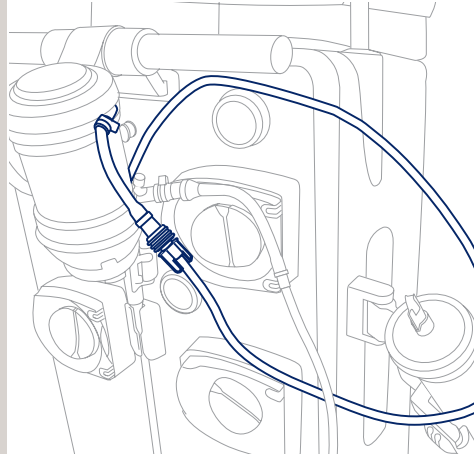
Step 2

The multiECCO2R is attached to the holder from above with the slot of the housing fitting into the nose of the holder. The yellow cap of the gas outlet (bottom left) can be removed.



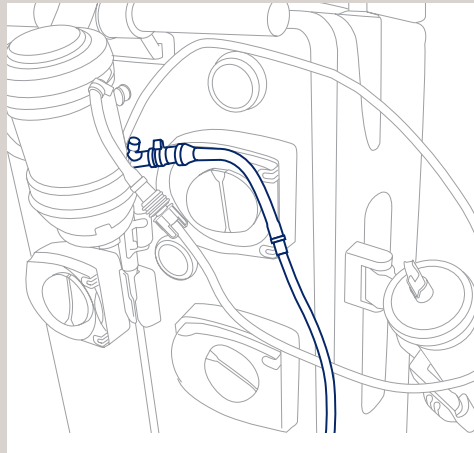
Step 3

The blood outlet of the multi**ECCO2R** (upper transparent screw top with white cap) is connected to the venous filter connection (blue) of the CKRT cassette system leading towards the bubble catcher.



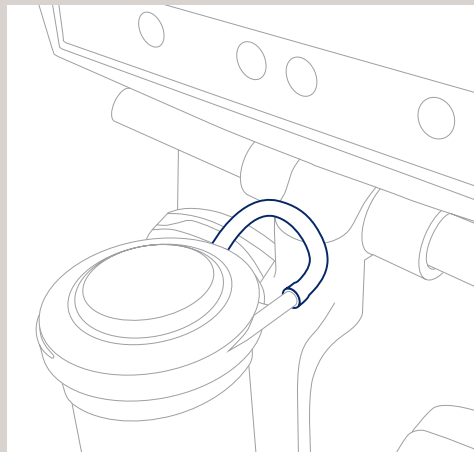
Step 4

The blood inlet of the multi**ECCO2R** (lower white long line with blue connector) is connected to the venous outlet of the hemofilter.



Step 5

The sweep gas line is connected to the outlet of the air/gas source (if required with additional flow regulator) and attached to the gas inlet with the green cap at the top of the multi**ECCO2R**. The multi**ECCO2R** is now ready for operation.



Patient access and anticoagulation with the multiECCO2R

Acute dialysis is a standard procedure in the intensive care unit

Extensive experience with CKRT systems as opposed to specific extracorporeal support systems

multiECCO2R can be operated with the vascular access used for CKRT

- Less invasive compared to conventional ECCO₂R
- Blood-gas exchanger used in series with CKRT filter²¹

Anticoagulation is a crucial element of ECCO₂R

- Bleeding risk with ECCO₂R requires careful evaluation of the benefit-risk ratio⁴
- The high rate of bleeding events with heparin-based anticoagulation in ECCO₂R calls for an improved anticoagulation regime¹⁴

multiECCO2R is the only available ECCO₂R system with optional citrate anticoagulation

Combination of multiFiltratePRO and multiECCO2R allows for usage of citrate-based anticoagulation

Technical data

Blood pump	Roller pump of CKRT machine
Blood flow rate of blood-gas exchanger	100–500 ml/min
Maximum ratio of gas/blood flow	15:1
Gas exchange membrane surface area	1.35 m ²
Coating of gas exchange membrane	Phosphorylcholine
Static blood priming volume	105 ml
Blood inlet	Female filter connector according to ISO 8637-2
Blood outlet	Male filter connector according to ISO 8637-1
Sterilized by	Ethylene oxide

Ordering information

multi ECCO2R gas exchanger	F00008943
Holder for multi Filtrate	F00007775
Holder for multi FiltratePRO	F00014754



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