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Effect of Impeller Design and Spacing on Gas Exchange in a Percutaneous Respiratory Assist Catheter

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Abstract

Providing partial respiratory assistance by removing carbon dioxide (CO₂) can improve clinical outcomes in patients suffering from acute exacerbations of chronic obstructive pulmonary disease and acute respiratory distress syndrome. An intravenous respiratory assist device with a small (25 Fr) insertion diameter eliminates the complexity and potential complications associated with external blood circuitry and can be inserted by nonspecialized surgeons. The impeller percutaneous respiratory assist catheter (IPRAC) is a highly efficient CO₂ removal device for percutaneous insertion to the vena cava via the right jugular or right femoral vein that utilizes an array of impellers rotating within a hollow-fiber membrane bundle to enhance gas exchange. The objective of this study was to evaluate the effects of new impeller designs and impeller spacing on gas exchange in the IPRAC using computational fluid dynamics (CFD) and in vitro deionized water gas exchange testing. A CFD gas exchange and flow model was developed to guide a progressive impeller design process. Six impeller blade geometries were designed and tested in vitro in an IPRAC device with 2- or 10-mm axial spacing and varying numbers of blades (2–5). The maximum CO₂ removal efficiency (exchange per unit surface area) achieved was 573 ± 8 mL/min/m² (40.1 mL/min absolute). The gas exchange rate was found to be largely independent of blade design and number of blades for the impellers tested but increased significantly (5–10%) with reduced axial spacing allowing for additional shaft impellers (23 vs. 14). CFD gas exchange predictions were within 2–13% of experimental values and accurately predicted the relative improvement with impellers at 2- versus 10-mm axial spacing. The ability of CFD simulation to accurately forecast the effects of influential design parameters suggests it can be used to identify impeller traits that profoundly affect facilitated gas exchange.

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Conflict of Interest:

None.

Keywords

Acute respiratory distress syndrome; Artificial lungs; Blood oxygenator; Chronic obstructive pulmonary disease; CO₂ removal; Gas exchange; Impeller design

The benefit of providing partial respiratory support (CO₂ removal) for patients with acute hypercapnic respiratory failure has been demonstrated with extracorporeal CO₂ removal (ECCO₂R) devices (1,2). Similar to extracorporeal membrane oxygenators (ECMOs), ECCO₂R systems utilize microporous hollow-fiber membranes (HFMs) to remove CO₂ and add oxygen (O₂) to the blood (3–5). By these means, the ECCO₂R device performs respiratory function independently of the pulmonary system, allowing the injured lungs to rest and heal. Partial respiratory support can prevent the need for invasive mechanical ventilatory treatment in patients with acute exacerbations of chronic obstructive pulmonary disease and allows low-tidal-volume lung protective ventilation strategies to be utilized in treatment of acute respiratory distress syndrome (6,7). Concerns with ECCO₂R are similar to those regarding traditional ECMO, however, in that blood loop and equipment management can be highly complicated. Some emerging ECCO₂R systems are comparatively less complex to operate (8,9), but all still depend on passage of blood through an external flow loop and generally have a high surface area of synthetic material directly in contact with blood (10).

Several groups have previously investigated or are currently investigating development of an intravenous device for partial respiratory support (11–16). All of these devices use HFMs as in ECMO/ECCO₂R devices, but instead of removing blood from the body in an external circuit, intravenous devices are inserted percutaneously into the venous system (generally the inferior vena cava). As a result, intravenous respiratory assist devices also have the advantage of performing respiratory function independently of the lungs, allowing the injured pulmonary tissue to rest and heal. In contrast to ECMO/ECCO₂R, however, the complexities associated with blood flow loops and circuit management are eliminated along with the high blood-contacting surface area. Intravenous devices also do not require a circuit blood pump and have the benefit of performing gas exchange on systemic blood flow through the inferior vena cava (~2/3 cardiac output), whereas blood availability for gas transfer in extracorporeal devices is limited by circuit blood flow. The greatest challenge in development of this technology is achievement of sufficient gas transfer with the limited gas exchange surface area that can be incorporated into a device that functions within the venous system while minimizing insertion size (10). Early intravenous devices achieved CO₂ removal rates up to 40–70 mL/min (17,18) and reached human clinical trials (19), but concern surrounded the large diameters (32–50 Fr), which required specialized surgeons for insertion (19–21). To eliminate the need for surgical insertion we are seeking to develop an intravenous device with an insertion diameter of 20–25 Fr. The promising approach we are investigating to achieve this was first presented by Mihelc et al. and consists of a slender HFM bundle surrounding an array of rotating impellers to generate an “active mixing” effect (22). Active mixing improves mass transfer by increasing blood velocity across gas exchange surfaces, which reduces the diffusive boundary layer thickness on the membrane surface and prevents blood-side accumulation of oxygen and depletion of carbon dioxide at

the membrane surface (23). This maintenance of a strong gas partial pressure differential across the membrane promotes efficient gas exchange. The impeller percutaneous respiratory assist catheter (IPRAC) achieved CO₂ removal rates up to 529 ± 20 mL/min/m² on the bench with a total fiber surface area of 0.07 m², for a total removal rate of 36 mL/min during pilot studies (22). Earlier work focused primarily on characterizing the relationship between rotation rate and gas exchange, as well as evaluation of eight different impeller designs. Not surprisingly, gas exchange correlated directly with rotation rate, and maximum CO₂ removal rates were achieved at the highest rate tested (20 000 rpm) (22). A strong dependence of gas exchange on impeller design was also observed. The top-performing design achieved exchange rates over twice that of the lowest performer. Recognizing the potential for further improvement to gas exchange, the objective of this work was to combine bench work and computational fluid dynamics (CFD) to develop and evaluate several new impeller designs for the IPRAC. We additionally investigated the effects on gas exchange of features such as axial spacing between impellers and number of blades.

MATERIALS AND METHODS

Device

The IPRAC prototype (Fig. 1A) consists of an array of impellers fixed to a flexible stainless steel driveshaft (0.042" [1.07-mm] diameter; SS304V, Heraeus Medical Components, St. Paul, MN, USA) that rotate concentrically within a stationary stainless steel coil (inner diameter 5 mm). Two hundred fifty polypropylene fibers (Membrana Celgard x30–240, Celgard, Wuppertal, Germany) are wrapped around the outside of the coil, preventing direct contact between impellers and fibers (Fig. 2A). Individual fibers have outer diameters of 300 μ m and measure 30 cm in length, for a total membrane surface area of 0.07 m². The flexible driveshaft extends out of the fiber bundle through the medial manifold, where it connects to an external DC brushless servomotor (2444-024B; MicroMo Electronics, Inc., Clearwater, FL, USA) at the proximal manifold. To prevent backflow of fluid up the driveshaft tubing, an infusion line continually pumps fluid at 15 mL/h down the driveshaft tube toward the medial manifold, where it exits the device into the recirculating loop. The sweep gas pathway in the full IPRAC prototype incorporates both the inlet and outlet gas ports in the proximal manifold, permitting percutaneous insertion to the inferior vena cava via the femoral vein (Fig. 2C). Sweep gas enters the inlet port and flows directly into the fiber bundle at the medial manifold. Sweep flow exits the fiber bundle in the distal manifold, where it enters separate tubing integrated into the fiber bundle that returns it to the gas outlet port in the proximal manifold. This return gas pathway consists of wire-reinforced polyimide tubing (MinVasive Components, Trenton, GA, USA). This design is different from that described by Mihelc et al., which used a hollow driveshaft tube to return the sweep gas from the distal to proximal manifold. This modification allows the diameter of the impeller driveshaft to be significantly reduced versus previous prototypes.

In this work, a modified IPRAC device (Fig. 1B) was used to evaluate gas exchange of each impeller. In vitro testing does not require percutaneous insertion, so the gas pathway was configured to allow sweep gas to exit directly from the distal manifold, thereby eliminating the need for return gas pathway tubing. The modification also allowed the impeller

driveshaft to be easily interchanged. This enabled the use of the same fiber bundle for all testing, thereby eliminating a potential source of variability. The sweep gas pressure at the fiber bundle inlet is consistent in both gas pathway designs, so the modification has no effect on resulting gas exchange.

Following initial testing, the impellers with greatest CO₂ removal rates in the modified IPRAC were incorporated into full IPRAC prototypes for gas exchange evaluation.

Impellers

All impellers were designed in SolidWorks (Concord, MA, USA) and fabricated at the University of Pittsburgh Swanson Center for Product Innovation (Pittsburgh, PA, USA) from a hydrophobic epoxy resin (Watershed XC11122, DSM Somos, Sittard, the Netherlands) using stereolithography. Impellers measured 10 mm in length with a maximum outer diameter of 4 mm. The reduction in driveshaft diameter from 0.090" (2.3 mm) in previous work to 0.042" (1.07 mm) allowed design of taller blades with increased surface area. The six impeller blade designs evaluated are shown in Fig. 3. The flat-blade design is similar to the top-performing geometry from previous work but has a threefold larger blade surface area to enhance potential fluid volume displacement. The curved, flat-tangent, and radial-tangent blades (where the radial-tangent design is a combination of the curved and flat-tangent blades) were designed with the objective of minimizing the change in velocity vector directionality of incident flow. The crescent blade was designed to funnel flow toward the center of the impeller, with the objective of focusing generated flow to a single region on each blade. All impellers had 2–5 blades. Impellers were glued to the distal 280 mm of flexible driveshafts. Axial separation distance between impellers was set at 2 or 10 mm, resulting in a total of 23 or 14 impellers, respectively.

Design of blades and determination of the optimal combination of blade design, axial spacing, and number of blades was a progressive process. The flat, flat-tangent, curved, and flat-tapered impellers were designed and tested first with four blades and 10-mm axial separation. Depending on whether design characteristics and arrangements were shown experimentally and in CFD simulations to be beneficial for gas exchange (e.g., axial separation, 45° taper on blade ends, etc.), these features were selectively implemented in later designs (i.e., radial-tangent and crescent blades). As a result, not all designs were tested with a varying number of blades or at multiple axial separation distances. The combinations of blade number and impeller spacing for the geometries tested are listed in Table 1.

In vitro flow loop and gas exchange testing

Gas exchange testing was performed in an in vitro recirculation loop (Fig. 4), as described by Eash et al. (21). The loop consisted of a reservoir, centrifugal pump (BPX-80; Medtronic, Minneapolis, MN, USA), two commercial oxygenators (Vision Hollow Fiber Oxygenator; Gish Biomedical, Rancho Santa Margarita, CA, USA) to control inlet CO₂ gas tension, and the modified IPRAC device within a 7/8-inch-internal diameter acrylic test section. Pure O₂ sweep gas was pulled through the fiber bundle at 3.0 L/min by a sealed vacuum pump (N811 KV.45P; KNF Neuberger, Inc., Trenton, NJ, USA) and regulated with a thermal mass flow

controller (GR-116-1-A-PV-O2; Fathom Technologies, Georgetown, TX, USA). Pressure drop across the fiber bundle was monitored with differential transducers (143C; Honeywell International, Inc., Morristown, NJ, USA). We have shown previously that measured CO₂ removal in water bench testing correlates well with in vivo performance (within ~10%) for IPRAC devices, so for simplicity all testing was performed in deionized water at 37°C (22,23). Water flow rate was maintained at 3.0 L/min in the loop and monitored with a clamp-on ultrasonic flow probe (Transonic Systems, Inc., Ithaca, NY, USA). Water pressure at the test section inlet was measured with a liquid pressure transducer (PX771-025DI; Omega Engineering, Inc., Stamford, CT, USA) and maintained at physiologically relevant venous pressures (10–15 mm Hg).

The CO₂ and O₂ gas tensions in the fluid were measured with a blood gas analyzer (RapidLab 248; Siemens, Erlangen, Germany). Inlet $p\text{CO}_2$ was adjusted to conditions relevant to venous blood ($p\text{CO}_2 = 50 \pm 5$ mm Hg) via a CO₂/N₂ gas mixture through commercial oxygenators. The outlet sweep gas CO₂ concentration was measured with a gaseous CO₂ analyzer (WMA-4; PP Systems, Amesbury, MA, USA). Inlet O₂ partial pressure was not regulated but was typically steady around 25 ± 10 mm Hg.

Gas exchange was evaluated for each impeller rotating at 20 000 rpm. The fraction of CO₂ in the outlet gas was used to calculate total CO₂ removal (V_{CO_2}) according to Eq. 1, as the product of the fraction of CO₂ exiting the fibers (F_{CO_2}) and the STP-corrected mass flow rate of the sweep gas ($Q_{\text{OUT}}^{\text{STP}}$).

$$V_{\text{CO}_2} = Q_{\text{OUT}}^{\text{STP}} F_{\text{CO}_2} \quad (1)$$

To reduce variability associated with small differences (<3 mm Hg) between trials, V_{CO_2} was then normalized ($V_{\text{CO}_2}^*$) to our target inlet $p\text{CO}_2$ of 50 mm Hg according to Eq. 2.

$$V_{\text{CO}_2}^* = V_{\text{CO}_2} \times \frac{50 \text{ mm Hg}}{p\text{CO}_2^{\text{INLET}}} \quad (2)$$

CFD flow model

Fluent 12.0 (ANSYS, Inc., Canonsburg, PA, USA) was used to solve the unsteady Reynolds-averaged incompressible laminar Navier–Stokes equations. Water was modeled as a single-phase Newtonian fluid with a viscosity of 0.8 cP. The fiber bundle was approximated by a porous media model using the Ergun relationship for fluid flow through packed columns (24) with porosity and permeability constants derived from Pacella et al. (25). While the Ergun approximation was strictly developed for packed beds of spherical particles, several groups have demonstrated its accuracy for simulating oxygenator fiber bundle flow (26–28). The base mass transport model developed by Zhang et al. (28) was employed for CO₂ gas exchange using the effective diffusivity established by Vaslef et al. (29). The spatially varying mass transfer coefficients for CO₂ transport were adapted from Svitek and Federspiel (23). Each CFD case consisted of a fluid reference frame rotating at

20 000 rpm with five impeller units (rotor, fiber bundle, outer test section) concatenated together with final CFD results scaled to match the actual device length. The simulation results were used to generate predicted CO₂ removal rates and flow velocity fields in and around the IPRAC.

Statistical analysis

Reported gas exchange values are the average of 6–8 measurements each. Significance testing was performed in PASW Statistics 18 (IBM, Armonk, NY, USA). Student's or paired *t*-tests and ANOVA were conducted with subsequent post hoc testing when all assumptions for parametric testing were satisfied. Assumptions required for parametric analysis included (i) homogeneity of variance (i.e., homoskedasticity) as determined with Levene's test; (ii) normally distributed data (Kolmogorov–Smirnov test); and (iii) equal group sample sizes. With violation of the first assumption, or if both the second and third assumption were violated, the nonparametric Kruskal–Wallis test was used in place of ANOVA. Nonparametric post hoc comparisons of means were conducted with the Mann–Whitney *U*-test coupled with a Bonferroni correction to avoid inflation of a Type I (false positive) error rate.

RESULTS

Spacing effects

The flat and flat–tapered blades were each tested side-by-side with 2-mm and 10-mm axial separation to investigate spacing effects on gas exchange efficiency. A small (5–10%) improvement in CO₂ removal rate ($P < 0.005$) was achieved at 2-mm separation for both geometries tested (Fig. 5A). Normalizing the gas exchange rate to the number of impellers (Fig. 5B) showed that reducing the separation gap resulted in 35% (flat blade) and 28% (flat–tapered blade) decreases in gas exchange per impeller.

Comparison of impeller blade designs

Six unique impeller designs were compared with either 10-mm (Fig. 6A) or 2-mm (Fig. 6B) axial separation with four blades each. Due to the progressive nature of the testing process, not all designs were evaluated at both 10- and 2-mm separation. The curved and flat–tangent blades were not shown to significantly affect gas exchange versus the flat blade at 10-mm separation, so they were not tested later at 2-mm separation after it was determined the shorter axial spacing was beneficial. The radial–tangent and crescent blades, which were designed last, were only tested at the more advantageous 2-mm separation distance. The curved and flat–tangent blades outperformed the flat–tapered blade in gas exchange testing by a small (5–8%) but statistically significant ($P < 0.005$) margin. No other designs were found to differ statistically with 10-mm separation; however comparison of flat and flat–tapered blades failed to meet the required *P* value by a small margin ($P = 0.009$, but required *P* value from Mann–Whitney nonparametric comparison of means with Bonferroni correction was $P < 0.0083$). Statistical comparison of means found the measured CO₂ removal data for the flat, flat–tapered, radial–tangent, and crescent blades (2-mm axial spacing) to differ insignificantly ($P = 0.072$), suggesting no statistical difference exists between these designs.

The 45° chamfer (taper) that distinguishes the flat and flat-tapered designs was not shown to affect gas exchange experimentally at either 2-mm or 10-mm separation. As no disadvantage in gas exchange was demonstrated for the tapered blade modification, this feature was incorporated into blades designed after that finding (i.e., crescent and radial-tangent).

Number of blades

Three designs (flat-tapered, radial-tangent, and crescent) were tested with varying numbers of blades (Fig. 7). The achievable gas exchange rates with the flat-tapered and crescent impellers were both found to be independent of the number of blades in head-to-head comparisons ($P = 0.24$ and $P = 0.97$, respectively). Only the radial-tangent impellers achieved statistically differing gas exchange rates ($P = 0.01$). CO₂ removal rates of the radial-tangent design with two blades were 5% ($P = 0.006$) and 4% ($P = 0.015$) less than the same design with three blades and four blades, respectively. While gas exchange rates were shown to differ statistically for one design with varying numbers of blades (radial-tangent), the overall effect for all devices tested was marginal (~0–5%).

Full IPRAC prototype gas exchange testing

Following in vitro gas exchange testing with the modified catheter device, full IPRAC prototypes were manufactured that incorporated impellers with either the crescent, flat-tapered, or radial-tangent blades. Each device consisted of impellers with three blades and 2-mm axial spacing. The gas exchange performances of the full IPRAC devices are shown in Fig. 8. The highest CO₂ removal rate (573 ± 8 mL CO₂/min/m²) was achieved with the crescent blade, followed by the flat-tapered (535 ± 17 mL CO₂/min/m²) and the radial-tangent (516 ± 7 mL CO₂/min/m²) prototypes. With the exception of the crescent blade, which achieved 11% greater CO₂ removal in a full IPRAC device versus the modified catheter, the gas exchange data generally agreed between full and modified IPRAC devices. In full prototypes the flat-tapered and radial-tangent blades performed 6 and 3% better than in testing with the modified device.

CFD simulations

Model predictions were conducted that corresponded to each in vitro test to forecast CO₂ removal rates and generated velocity fields. The flow generated in and out of the fiber bundle and external flow space by impeller rotation is shown in Fig. 9. The velocity contours show that fluid is propelled radially outward due to rotation and recirculates radially inward from the external flow space toward the shaft in the space between impellers. The velocity of inward flow is inversely proportional to the impeller axial separation distance. The recirculating behavior of flow in and out of the fiber bundle results in blood being exposed to gas exchange surfaces several times before it traverses the entire length of the device.

The predicted CO₂ removal rates of each blade design are shown with corresponding in vitro removal rates in Fig. 10. Predicted exchange rates generally agreed with experimental data (within 2–13% for all comparisons). The model accurately forecast that removal rates for impellers with 2-mm axial spacing would exceed those at 10-mm spacing. The reduced efficiency at the shorter axial spacing was also well predicted. The predicted reduction in

CO₂ removal per impeller at 2-mm versus 10-mm spacing in CFD simulations differed from in vitro measurements by ~5%. The model predicted that blade designs would yield a range of gas exchange differences between 5 and 10%; however, in all but two instances our experimental data failed to discriminate the removal rates achieved by each design with statistical significance. In each of those two instances (flat–tangent vs. flat–tapered and curved vs. flat–tapered) the model accurately predicted the trend measured experimentally (measured: both designs 5–8% better than flat–tapered; predicted: both designs 7% better than flat–tapered).

Based on observations from CFD flow velocity simulations, a 45° chamfer (taper) was incorporated into some blade designs. The modification was intended to eliminate flow interference in the space between impellers that contributed to increased resistance to radially inward flow when arranged with 2-mm axial spacing. The predicted benefit of the modification is shown by qualitative comparison of the velocity fields generated by the flat blade with those generated by the flat–tapered blade in Fig. 9. By incorporating the 45° taper into the flat–tapered design (the only difference between it and the flat blade), the region of high-velocity radially outward flow increased in size and penetration distance through the fiber bundle. Similarly, the predicted CO₂ removal rate using the flat–tapered design at 2-mm axial spacing exceeded that for the flat blade design, despite the model predicting the opposite with 10-mm axial spacing. Experimentally, the beneficial effects of the modification were not demonstrated to be statistically significant, as discussed above (i.e., flat differed from flat–tapered insignificantly at both 2- and 10-mm spacing); however, we can conclude that no disadvantage in gas exchange at 2-mm spacing was found. In addition to the qualitative reduction in flow interference between impeller blades at 2-mm spacing observed in CFD simulations, the modification was incorporated into designs following these outcomes (i.e., crescent and radial–tangent).

DISCUSSION AND CONCLUSIONS

Both our predictive CFD model and in vitro testing demonstrated that CO₂ removal achieved with impeller rotation was improved by reducing axial spacing and increasing the total number of rotating impellers. The design of the blade and the number of blades on each impeller were not found to significantly influence gas exchange. Our top-performing impeller arrangement achieved a CO₂ removal rate of 573 ± 8 mL/min/m² (40.1 mL/min) in a full IPRAC device, an improvement of ~10% versus previous work (22).

The mechanisms by which an actively mixed system can facilitate HFM-mediated gas exchange in blood oxygenators have been described previously (23,30–32). In short, impeller rotation adds orthogonal velocity components to bulk movement in the vessel, resulting in cross-flow through the fiber bundle and increased fluid velocity at the membrane surface. Greater velocity and bundle cross-flow diminish the highly limiting diffusive boundary layer at the gas exchange surface, facilitating maintenance of stronger gaseous concentration gradients spanning fiber walls (30). The significance of this enhancement is emphasized when considering the effect of impeller-facilitated active mixing on the mass exchange effectiveness parameter. The ratio (~0–1) of achieved CO₂ removal versus maximum possible removal normalized for blood flow rate, gas flow rate, and $p\text{CO}_2^{\text{INLET}}$

increases >15-fold from 0.012 to 0.203 with impeller rotation at 20 000 rpm versus passive gas exchange (i.e., 0 rpm) (33).

Among potential factors contributing to gas exchange, our results suggest that indirect and direct interactions between neighboring impellers are of importance. When axial separation distance is reduced from 10 to 2 mm, the length of the fiber bundle associated with each impeller (i.e., bundle length/number of impellers) decreases by 40%. We believe the CO₂ removal efficiency of each impeller (i.e., $V_{CO_2}^*/A/\text{Number of impellers}$) with 2-mm axial spacing is affected by the reduced bundle surface area associated with each impeller. Figure 9 shows CFD-predicted velocity profiles in fluid surrounding impellers and the flow pathways of fluid as affected by rotating impellers. Above each rotor, fluid is strongly propelled radially outward through the fiber bundle before recirculating inward back through the bundle in the space between impellers. As the distance between impellers shrinks, the resistance to inward flow increases, reducing the pumping efficiency of each impeller and the associated contribution to gas exchange. In simulations we demonstrated that a 45° chamfer at the blade ends mitigated this interference and diminished the losses in efficiency for individual impellers at 2- versus 10-mm spacing (22% predicted improvement in CO₂ removal at 2 vs. 10 mm for flat–tapered, 16% for flat). Experimentally, the modification did not significantly affect overall gas exchange (i.e., the flat and flat–tapered blades did not differ statistically at 2-mm spacing or at 10-mm spacing), but the improvement in total CO₂ removal at 2-mm spacing versus 10-mm spacing for the flat–tapered blade (18%) exceeded that for the flat blade (7%). The effects of the blade taper are logically not inclusive of gas exchange and could possibly contribute a hemocompatibility advantage as well, given that attenuating flow interference may lessen stresses exerted on blood cells. Given that our overall gas exchange improved with 23 versus 14 impellers despite the 28–34% reduced contribution of individual impellers, we proceeded with testing of new blade designs (crescent and radial–tangent) exclusively at 2-mm spacing. Considering the potential benefits to gas exchange and hemocompatibility, each was designed with a 45° taper at the end of each blade.

Each impeller chosen for testing in full IPRAC prototypes was fabricated with three blades. The failure to show any significant effect of blade number on gas exchange for the designs tested suggests that only a few impeller blades provide the necessary orthogonal velocity components required to create efficacious active mixing conditions. We also theorized that additional blades would exert additional shear stresses and viscous energy dissipation to the fluid. Given the conceivable advantage to hemocompatibility and equivalent contribution to gas exchange, we concluded that incorporating more than three blades was inessential. The discrepancy in performance between the modified and full IPRAC devices containing the same impellers/arrangements may be due in part to the manufacturing process, given that the fiber bundle is wrapped and potted for each device by hand.

The CFD simulation model developed for the IPRAC was valuable for flow visualization and drove our progressive design process. Formal optimizations of impeller blade designs were not conducted, however. A limitation of developing a CFD model for a complex flow system such as the IPRAC is that not all nuances of device operation can be captured with

exact fidelity. For example, the use of a nonrigid driveshaft that provides the IPRAC with the necessary flexibility for insertion and operation in tortuous environments does not prevent radial impeller movement within the safety coil. It is possible that operational subtleties such as this affect resulting gas exchange non-negligibly, but they would be far too complex to accurately predict in a CFD model. Despite this, the error associated with our gas exchange model was reasonably acceptable (2–13%), and the model accurately predicted the overall benefits of reducing impeller axial spacing, which we demonstrated to be the most influential parameter investigated. This finding suggests that our model may be beneficial in future studies for identifying design features and impeller arrangements that profoundly influence gas exchange.

Rotation speed remains an important factor in active mixing, as was shown for all geometries tested previously (22). Other possible design parameters or arrangements that may contribute to gas exchange that were not investigated in this work are impeller length and driveshaft orientation relative to other impellers (i.e., whether the impeller is aligned with blades offset to neighboring impeller). Collectively, though, these results suggest that at constant impeller rotation rates, we may expect little further improvement in gas exchange with optimization of impeller blade designs and arrangements.

Future studies specific to the catheter design will focus on establishment of hemocompatibility. Basic shear stress predictions from our computational model were used to estimate blood trauma generated from impeller rotation (data not shown). Normalized index of hemolysis (NIH) calculations, indicating the estimated grams of hemoglobin released to plasma per 100 L of blood flow, did not exceed 0.005 g/100 L for any impeller or arrangement evaluated. NIH values at this level are considered acceptable when compared with clinically available oxygenator devices (34,35); however, conclusive in vitro testing has not been completed to verify or dispute the CFD predictions. Subsequent to all in vitro testing, both gas exchange and hemocompatibility of full IPRAC prototypes will be verified in acute in vivo bovine studies.

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REFERENCES

1. Kaushik M, Wojewodzka-Zeleznikowicz M, Cruz DN, et al. Extracorporeal carbon dioxide removal: the future of lung support lies in the history. *Blood Purif.* 2012; 34:94–106. [PubMed: 23095408]
2. Habashi NM, Borg UR, Reynolds HN. Low blood flow extracorporeal carbon dioxide removal (ECCO₂R): a review of the concept and a case report. *Intensive Care Med.* 1995; 21:594–597. [PubMed: 7593903]
3. Bigatello LM, Stelfox HT, Berra L, Schmidt U, Gettings EM. Outcome of patients undergoing prolonged mechanical ventilation after critical illness. *Crit Care Med.* 2007; 35:2491–2497. [PubMed: 17901840]

4. Pesenti A, Patroniti N, Fumagalli R. Carbon dioxide dialysis will save the lung. *Crit Care Med*. 2010; 38(Suppl. 10):S549–S554. [PubMed: 21164396]
5. Thourani VH, Kisrhbom PM, Kanter KR, et al. Venoarterial extracorporeal membrane oxygenation (VA-ECMO) in pediatric cardiac support. *Ann Thorac Surg*. 2006; 82:138–145. [PubMed: 16798204]
6. Cove M, MacLaren G, Federspiel W, Kellum J. Bench-to-bedside review: extracorporeal carbon dioxide removal, past present and future. *Crit Care*. 2012; 16:232. [PubMed: 23014710]
7. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000; 342:1301–1308. [PubMed: 10793162]
8. Arazawa DT, Oh H-I, Ye S-H, et al. Immobilized carbonic anhydrase on hollow fiber membranes accelerates CO₂ removal from blood. *J Memb Sci*. 2012; 403–404:25–31.
9. Batchinsky AI, Jordan BS, Regn D, et al. Respiratory dialysis: reduction in dependence on mechanical ventilation by venovenous extracorporeal CO₂ removal. *Crit Care Med*. 2011; 1:1382–1387. [PubMed: 21317644]
10. Federspiel, WJ.; Svitek, RG. Lung, artificial: current research and future directions. In: Wnek, GE.; Bowlin, GL., editors. *Encyclopedia of Biomaterials and Biomedical Engineering*. New York: Marcel Dekker; 2004. p. 922–931.
11. Mortensen JD, Berry G. Conceptual and design features of a practical, clinically effective intravenous mechanical blood oxygen/carbon dioxide exchange device (IVOX). *Int J Artif Organs*. 1989; 12:384–389. [PubMed: 2777397]
12. Macha M, Federspiel WJ, Lund LW, et al. Acute in vivo studies of the Pittsburgh intravenous membrane oxygenator. *ASAIO J*. 1996; 42:M609–M615. [PubMed: 8944953]
13. Makarewicz AJ, Mockros LF, Anderson RW. A pumping intravascular artificial lung with active mixing. *ASAIO J*. 1993; 39:M466–M469. [PubMed: 8268580]
14. Snider MT, High KM, Richard RB, et al. Small intrapulmonary artery lung prototypes: design, construction, and in vitro water testing. *ASAIO J*. 1994; 40:M533–M539. [PubMed: 8555573]
15. Cattaneo G, Strauß A, Reul H. Compact intra- and extracorporeal oxygenator developments. *Perfusion*. 2004; 19:251–255. [PubMed: 15376770]
16. Kim G-B, Kwon T-K, Hung C-U. Design of an intravenous oxygenator. *J Artif Organs*. 2006; 9:34–41. [PubMed: 16614800]
17. Zwischenberger JB, Tao W, Bidani A. Intravascular membrane oxygenator and carbon dioxide removal devices: a review of performance and improvements. *ASAIO J*. 1999; 45:41–46. [PubMed: 9952005]
18. Eash HJ, Frankowski BJ, Hattler BG, Federspiel WJ. Evaluation of local gas exchange in a pulsating respiratory support catheter. *ASAIO J*. 2005; 51:152–157. [PubMed: 15839440]
19. Conrad SA, Bagley A, Bagley B, et al. Major findings from the clinical trials of the intravascular oxygenator. *Artif Organs*. 1994; 18:846–863. [PubMed: 7864735]
20. Conrad SA, Eggerstedt JM, Morris VF, Romero MD. Prolonged intracorporeal support of gas exchange with an intravenacaval oxygenator. *Chest*. 1993; 103:158–161. [PubMed: 8417871]
21. Eash HJ, Mihelc KM, Frankowski BJ, Hattler BG, Federspiel WJ. Evaluation of fiber bundle rotation for enhancing gas exchange in a respiratory assist catheter. *ASAIO J*. 2007; 53:368–373. [PubMed: 17515731]
22. Mihelc KM, Frankowski BJ, Lieber SC, Moore ND, Hattler BG, Federspiel WJ. Evaluation of a respiratory assist catheter that uses an impeller within a hollow fiber membrane bundle. *ASAIO J*. 2009; 55:569–574. [PubMed: 19779302]
23. Svitek RG, Federspiel WJ. A mathematical model to predict CO₂ removal in hollow fiber membrane oxygenators. *Ann Biomed Eng*. 2008; 36:992–1003. [PubMed: 18347984]
24. Ergun S. Fluid flow through packed columns. *Chem Eng Prog*. 1952; 49:89–94.
25. Pacella HE, Eash HJ, Frankowski BJ, Federspiel WJ. Darcy permeability of hollow fiber bundles used in blood oxygenation devices. *J Memb Sci*. 2011; 382:238–242. [PubMed: 22927706]
26. Gage KL, Gartner MJ, Burgreen GW, Wagner WR. Predicting membrane oxygenator pressure drop using computational fluid dynamics. *Artif Organs*. 2002; 26:600–607. [PubMed: 12081518]

27. Gartner MJ, Wilhelm CR, Gage KL, Fabrizio MC, Wagner WR. Modeling flow effects on thrombotic deposition in a membrane oxygenator. *Artif Organs*. 2000; 24:29–36. [PubMed: 10677154]
28. Zhang J, Nolan TDC, Zhang T, Griffith BP, Wu ZJ. Characterization of membrane blood oxygenation devices using computational fluid dynamics. *J Memb Sci*. 2007; 288:268–279.
29. Vaslef SN, Mickros LF, Cook KE, Leonard RJ, Sung JC, Anderson RW. Computer-assisted design of an implantable, intrathoracic artificial lung. *Artif Organs*. 1994; 18:813–817. [PubMed: 7864729]
30. Mockros LF, Leonard R. Compact cross-flow tubular oxygenators. *Trans Am Soc Artif Intern Organs*. 1985; 31:628–633. [PubMed: 3837521]
31. Vaslef SN, Mockros LF, Anderson RW, Leonard RJ. Use of a mathematical model to predict oxygen transfer rates in hollow fiber membrane oxygenators. *ASAIO J*. 1994; 40:990–996. [PubMed: 7858338]
32. Wickramasinghe SR, Semmens MJ, Cussler EL. Mass transfer in various hollow fiber geometries. *J Memb Sci*. 1992; 69:235–250.
33. Turri F, Yanagihara JJ. Computer-assisted numerical analysis for oxygen and carbon dioxide mass transfer in blood oxygenators. *Artif Organs*. 2011; 35:579–592. [PubMed: 21671959]
34. Kawahito S, Maeda T, Yoshikawa M, et al. Blood trauma induced by clinically accepted oxygenators. *ASAIO J*. 2001; 47:492–495. [PubMed: 11575824]
35. Wu ZJ, Gellman B, Zhang T, Taskin ME, Dasse KA, Griffith BP. Computational fluid dynamics and experimental characterization of the pediatric pump-lung. *Cardiovasc Eng Technol*. 2011; 2:276–287. [PubMed: 24839468]

FIG. 1.

(A) Full IPRAC prototype suitable for percutaneous insertion with gas inlet and outlet at the proximal manifold. (B) Modified IPRAC used to compare in vitro CO₂ removal from water in an in vitro flow loop with distal manifold sweep gas outlet port and easily interchangeable impeller driveshaft.

FIG. 2.

(A) Cutaway view of IPRAC fiber bundle showing indwelling safety coil and impellers on driveshaft. (B) Enlarged view of sweep gas versus blood pathways in a single HFM. Pure O_2 gas flows into the fiber lumen and an $O_2 + CO_2$ gas mixture exits at fiber outlet. Blood flows on the outside of the fiber, separated from sweep gas flow by the microporous fiber wall. (C) IPRAC insertion to the inferior vena cava (IVC) via the femoral vein with percutaneous gas pathway and driveline tubing.

FIG. 3.

Six impeller geometries evaluated in in vitro gas exchange studies. Each impeller measures 10 mm in length with a maximum outer diameter of 4 mm.

FIG. 4.

In vitro recirculating flow loop used to evaluate gas exchange of modified IPRAC.

FIG. 5.

Spacing effects on gas exchange. All impellers were fixed to a 270-mm section of driveshaft at either 2- or 10-mm axial spacing between impellers. At the shorter (2-mm) and longer (10-mm) axial separation distances, 14 and 23 impellers were attached in total, respectively. Plots show CO₂ removal rates of flat and flat-tapered impellers (with four blades) at both 2- and 10-mm axial spacing with normalization for (A) fiber surface area (0.07 m²) or (B) fiber surface area and number of impellers. **P* < 0.05.

FIG. 6.

Effect of blade design on gas exchange. CO₂ removal rate normalized to fiber surface area (0.07 m²) of six impeller designs, each with four blades. (A) Data shown for impellers with 10-mm axial separation. (B) Data shown for impellers with 2-mm axial separation. ‡*P* < 0.05.

FIG. 7.

Effects of blade frequency on gas exchange. CO₂ removal rate normalized to fiber surface area (0.07 m²) versus blade number on impellers with (A) crescent blades, (B) radial-tangent blades, and (C) flat-tapered blades. Each impeller device had 2-mm axial separation. [†] $P < 0.001$, $**P < 0.05$.

FIG. 8. Measured CO₂ removal rates of IPRAC devices using either crescent, flat-tapered, or radial-tangent blade designs. Each impeller contained three blades and was separated axially from the others by 2 mm.

FIG. 9. CFD-predicted fluid velocities with 3 L/min of bulk flow from left to right. Light and dark contour regions correspond to fluid velocity (in m/s) in positive radial direction (away from shaft) and negative radial direction (toward the shaft), respectively. (A) Flat blade, 2-mm spacing. (B) Flat-tapered blade, 2-mm axial spacing.

FIG. 10.

CFD-predicted CO₂ removal rates normalized to fiber surface area (0.07 m²) plotted with modified IPRAC experimental data for various impeller designs and arrangements. Group nomenclature: impeller name (number of blades, impeller separation distance in millimeters).

TABLE 1

Design matrix showing combinations of parameters evaluated in vitro

Blade design	With 10-mm spacing (14 impellers)	With 2-mm spacing (23 impellers)
Flat	4 blades only	4 blades only
Flat-tapered	4 blades only	3, 4, or 5 blades
Flat-tangent	4 blades only	—
Curved	4 blades only	—
Radial-tangent	—	2, 3, or 4 blades
Crescent	—	3 or 4 blades