Evaluation of Plasma Resistant Hollow Fiber Membranes For Artificial Lungs

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Hollow fiber membranes (HFMs) used in artificial lungs (oxygenators) undergo plasma leakage (or wetting) in which blood plasma slowly fills the pores of the fiber wall, plasma leaks into gas pathways, and overall gas exchange decreases. To overcome this problem plasma resistant fibers are being developed that are skinned asymmetric or composite symmetric versions of microporous oxygenator fibers. This report evaluates several candidate plasma resistant HFMs in terms of their gas permeance and plasma resistance as measured in a surfactant wet out test. Five candidate fibers were compared with each other and with a control fiber. CO_2 and O_2 gas permeance (in ml/s/cm^2/cm Hg) in the plasma resistant fibers ranged from 3.15E-04 to 1.71E-03 and 3.40E-04 to 1.08E-03, respectively, compared with 1.62E-02 and 1.77E-02 for the control fiber. Maximum dye bleed through for the plasma resistant fibers in the forced wet out test were significantly less than for the control fiber. CO_2 gas permeance of a plasma resistant fiber imposes the greatest constraint upon artificial lung design for sufficient gas exchange. However, our results suggest sufficient plasma resistance can be achieved using special skinned and composite HFMs while maintaining an acceptable CO_2 gas permeance for a broad range of artificial lung applications. *ASAIO Journal* 2004; 50:491–497.

Clinical support for patients with acute respiratory failure, including acute exacerbation of a chronic disease such as chronic obstructive pulmonary disease (COPD), can be achieved using extracorporeal membrane oxygenation (ECMO)[1,2] or related artificial lung therapies. ECMO is often performed using standard blood oxygenators used in cardiopulmonary bypass,[3,4] which are composed of bundles of microporous hollow fiber membranes (HFMs) that allow for oxygenation and carbon dioxide removal from blood. Microporous hollow fiber membranes also form the basic gas exchange units of next generation artificial lungs being developed for improved respiratory support in acute and chronic lung failure. Strategies under development include semipermanent artificial lungs for complete respiratory support as potential bridges to lung transplant[5,6] and temporary artificial lung devices for partial acute respiratory support. Our group has been developing a respiratory support catheter, which uses a bundle of hollow fiber membranes temporarily inserted into the vena cava of patients with acute lung failure.[7–10]

Hollow fiber membranes used in artificial lungs are made from hydrophobic polymers so that the submicron pores spanning the fiber wall remain gas filled and promote rapid transmural gas diffusion. In contact with water, liquid intrusion into the fiber wall does not occur appreciably, and gas permeance of the fiber shows negligible decay with extended water contact.[11] In contact with blood, however, microporous fibers undergo plasma leakage (or plasma wetting), whereby blood plasma leaks into the fiber wall, filling wall pores with liquid and significantly impeding gas exchange. Plasma wetting generally occurs within 8–16 hours of blood contact.[12–14] Plasma leakage most likely occurs because bipolar phospholipids in blood adhere to the surface of the fiber, creating a hydrophilic layer at the pore surface, which gradually creates pathways for plasma intrusion into the pores.[14] Vapor condensation in wall pores caused by the temperature difference between the sweep gas flowing through the fiber and blood has also been proposed as another mechanism for plasma leakage,[15] but this hypothesis appears inconsistent with heat transfer analyses and studies of microporous hollow fibers in heated water.[11] Replacement of an oxygenator after significant plasma wetting may be an option in standard ECMO (albeit not a preferable one) but not for intracorporeal and other next generation artificial lungs for respiratory support, which should have improved long-term durability in terms of plasma wetting resistance compared with standard blood oxygenators.

Skinned asymmetric and composite symmetric microporous hollow fibers use layers of nonporous polymers as "skins" upon the surfaces of microporous hollow fiber membranes and are prime candidates for use in artificial lung applications.[16,17] The nonporous polymer layer blocks or impedes plasma infiltration into wall pores to help maintain gas diffusion (**Figure 1**). The challenge lies in developing a fiber or fiber composite that effectively resists plasma wetting but that does not reduce the overall gas permeance of the fibers necessary for sufficient gas exchange. In this study, we evaluate several candidate skinned and composite "plasma resistant" hollow fibers for next generation artificial lungs in terms of both gas permeance and plasma resistance as assessed through a model bench study of wetting. The study looks at commercially available plasma resistant fibers as well as a more gas permeable composite fiber, currently under development for our respiratory support catheter. The study addresses (1) the CO_2 and O_2 gas permeances of the plasma resistant fibers, including an analysis to determine which permeance imposes the greatest constraint upon the development of a plasma resistant fiber, and (2)

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Submitted for consideration March 2004; accepted for publication June 2004.

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DOI: 10.1097/01.MAT.0000138078.04558.FE

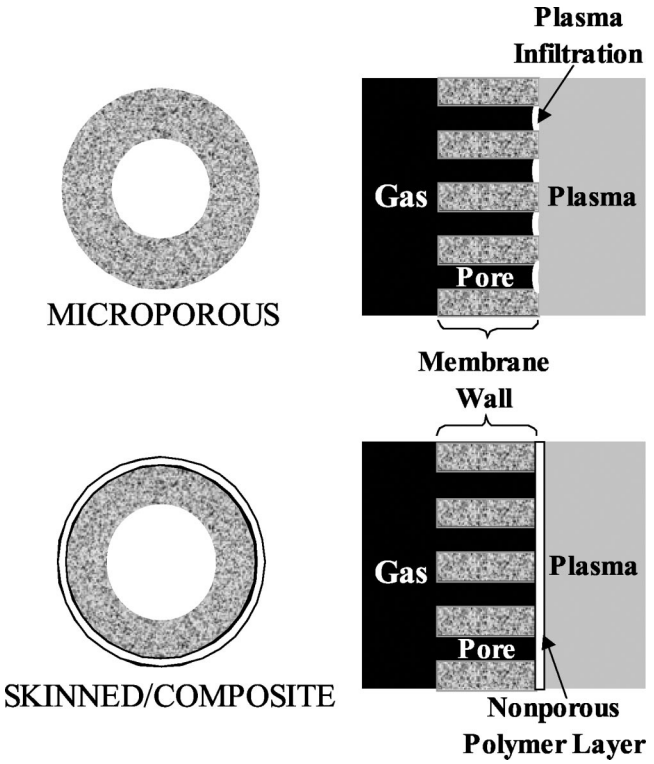

Figure 1. Nonporous polymer layers blocking plasma infiltration.

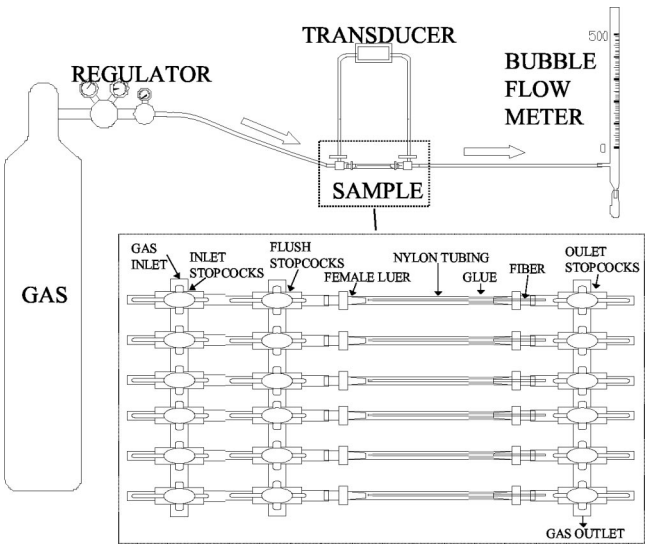

Figure 2. Gas-gas permeance schematic.

whether acceptable plasma resistance can be achieved without a significant reduction in gas permeance.

Materials and Methods

Table 1 summarizes the principal characteristics of the five different plasma resistant fibers evaluated in this study. The Celgard (Celgard Inc., Charlotte, NC)[18] ×30–240 fiber is a microporous symmetric hollow fiber that has increased "plasma resistance" compared with standard oxygenator fibers by virtue of a reduced pore size. The Celgard fiber served as our positive control for wetting studies because it is neither a skinned asymmetric nor a composite symmetric hollow fiber membrane. The Membrana fiber (Membrana, Wuppertal, Germany)[19] and the DIC II fiber (Dainippon Ink and Chemicals, Inc., Japan)[20] are skinned asymmetric fibers, whereas the Senko (Senko Medical Instrument Mfg., Tokyo, Japan)[21] fiber is a composite symmetric fiber; all are currently used in commercial extracorporeal oxygenators.[12,13,22–26] The AMT fiber (Applied Membrane Technology, Inc., Minnetonka, MN)[27] is a custom composite symmetric hollow fiber being developed as a more gas permeable plasma resistant hollow fiber for our respiratory support catheter. Both the AMT and Senko fibers use radio frequency glow discharge (RFGD) plasma polymerization of an ultra thin, nonporous siloxane layer on the Celgard ×30–240 polypropylene microporous hollow fiber.

Gas Permeance Studies

The gas permeance of each fiber for CO_2 and O_2 was evaluated in the apparatus shown in **Figure 2**. Fiber samples were evaluated in nylon tube test modules (n = 6), in which one end of the fiber was occluded with glue and the other end open to the gas outlet pathway. The nylon tube was sealed at the gas outlet end, causing the gas in the tube to permeate through the fiber. The length of fiber exposed to the test gas was measured for each module to calculate the exposed fiber surface area (SA). All six fiber modules were placed in parallel in the test setup for the tests at room temperature (23°C) (sets of three modules were submerged in a bath for tests at 37°C). The gas source (first O_2 and then CO_2) was regulated (pressure regulator, P/N P15–02–000, and pressure gauge [0–30 psi],

Table 1. Principle Characteristics of Plasma Resistant Fiber Candidates

Name	Material	Type	Substrate	ID (μm)	OD (μm)	Wall Thickness (μm)
Celgard	Polypropylene	Symmetric	N/A	240	300	30
Membrana	PMP (Polymethylpentene)	Skinned Asymmetric	N/A	200	380	90
DIC II	Poly-4-methyl-1-pentene	Skinned Asymmetric	N/A	165	225	30
Senko	TMCTS (1,3,5,7 tetramethylcyclotetrasiloxane)	Composite Symmetric	Polypropylene[a]	240	300	30
AMT	Siloxane	Composite Symmetric	Polypropylene[a]	240	300	30

[a] Celgard ×30240

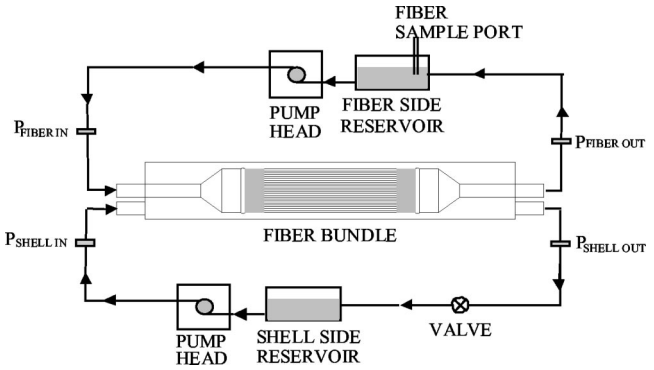

Figure 3. Surfactant forced wet-out schematic.

P/N PPA-95–107, Wilkerson Operations, Englewood, CO) and connected to the gas inlet of the modules. For 37°C, the gas pathway was coiled under the water before the module and temperature probes (Type T thermocouple, P/N 08505–90, and Digi-Sense type T thermocouple thermometer, P/N 91100–20, Cole-Parmer Instrument Company, Vernon Hills, IL) were placed immediately before and after the module to ensure that the test gas was at 37°C. A bubble flow meter (10 ml bubble meter, for high permeance, P/N 20562; capillary column bubble meter, for low permeance, P/N 23771, Supelco, Bellefonte, PA) was connected to the gas outlet of the modules. Transmural pressure (across the fiber wall) was measured using a pressure transducer (signal conditioned pressure transducer, P/N 143SC15D, SenSym Inc., Milpitas, CA) at the gas inlet and outlet.

All six fiber modules were flushed simultaneously for the 23°C tests (sets of three for the 37°C tests) with the test gas at 500 mm Hg for 10 minutes to ensure that the tube was entirely filled with the gas. Gas permeance measurements were made on the first module by closing the gas pathway to the other five modules. Then the gas flow path was changed to only go through the second module, and so forth for all remaining modules. Gas outlet flow rate was measured using a stopwatch and graduated bubble flow meter (flow measurements were adjusted to STP using $Q_2 = \left(\frac{P_1}{P_2}\right)\left(\frac{T_2}{T_1}\right)Q_1$, where 1 are the test conditions and 2 are STP conditions, temperature for the 37°C tests was measured using a temperature probe immediately before the bubble flow meter).

The gas permeance of the fiber in the test module was calculated using

$$K = \frac{Q}{SA \cdot \Delta P} \tag{1}$$

where K is the gas permeance, Q is the measured gas flow rate, SA is the computed surface area of fiber exposed to test gas, and ΔP is the differential pressure across the fiber wall (500 mm Hg for these studies).

Fiber Wetting Studies

The wetting resistance of the candidate fibers was assessed using a surfactant forced wet out test and a dye to monitor liquid bleed through across the fiber wall, as shown in **Figure 3**. Test fibers were potted onto both ends of a cylindrical core. Excess fiber was cut off the ends of the core, opening up the inner lumen of the fibers. The ends of the module were then connected to hollow metal end caps using pieces of polyurethane as seals. The whole test module was then placed into a tube, and the ends were placed through two holed rubber stoppers. A line placed through one of the holes was connected to the metal end cap, creating the fiber side pathway. The second line was exposed to the outside of the fibers (shell side pathway).

A 50/50 mixture of methylene blue dye in deionized (DI) water and isopropyl alcohol was used on the shell side as the wetting solution and pure DI water was used on the fiber side. Roller pumps (Masterflex L/S Easy Load pump head, P/N 07518–10, and Masterflex modular drive [1–100 rpm], P/N 07553–80, Cole-Parmer Instruments Company, Vernon Hills, IL) were used to circulate the fluids on both sides. Inlet and differential pressures for both sides were measured (differential pressure transducer, P/N PX771, and meter, P/N DP41-E, Omega, Stamford, CT), and shell side pressure was adjusted using a needle valve at the shell outlet to create an average transmural pressure across the fiber wall of 100 mm Hg in all fiber tests. The transmural pressure (ΔP_{TRANS}) was calculated using $\Delta P_{TRANS} = \bar{P}_S - \bar{P}_F$, where $\bar{P}_S$ and $\bar{P}_F$ are the average of inlet and outlet pressures, shell side and fiber side, respectively. Samples (1.5 ml) were taken from the fiber reservoir at various time points, and the absorbance of dye was measured spectrophotometrically (Genesys 5 UV-Vis spectrophotometer, P/N 336001, Thermo Spectronic, Rochester, NY) at 667 nm. The slope of dye concentration *versus* elapsed time for the plasma resistant fibers was calculated for each test (n =3) after 1 hour to eliminate initial nonlinear transients. The nonskinned/composite Celgard fiber's slope was calculated starting at t = 0 because of a faster rate of dye bleed through. The slope for each test was then normalized to wall thickness (to make it directly proportional to the resistance to water flow and liquid bridges formed in the pores), exposed fiber surface area, and transmural pressure (caused by up to a 10% difference in ΔP between experiments) using

$$m^* = \frac{m \cdot h}{SA \cdot \Delta P} \tag{2}$$

where m^* is the normalized slope, m is the unnormalized slope of dye concentration over elapsed time, h is the wall thickness of the test fiber, SA is the exposed fiber surface area, and ΔP is the transmural pressure of the test. The number of fibers varied from module to module because of manufacturing. The Celgard module contained 99 fibers. The three trials for the plasma resistant candidate fibers contained the following number of fibers: Membrana = 114, 111, and 109; DIC II = 181, 191, and 180; Senko = 88, 88, and 96; AMT #2452 = 94, 92, and 91; and AMT #2453 = 93, 95, and 93. Average normalized slopes for all fiber types were compared to determine the level of plasma resistance.

Statistical Analysis

Statistical comparisons were done using a Student's t-test, assuming equal sample variance. This method of analysis provided p-values for a specific set of comparisons. Differences were considered significant for $0.01 \leq p < 0.05$. P-values <

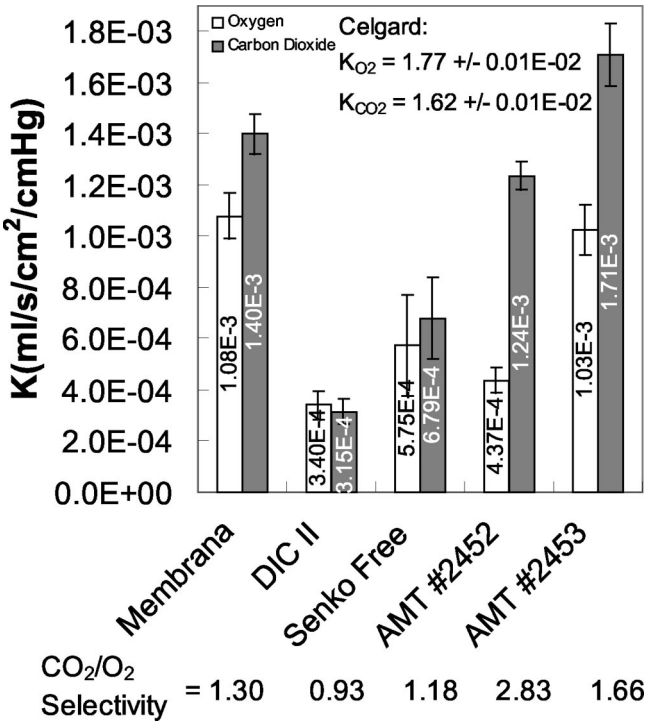

Figure 4. Gas permeance and CO_2/O_2 selectivity of candidate plasma resistant fibers.

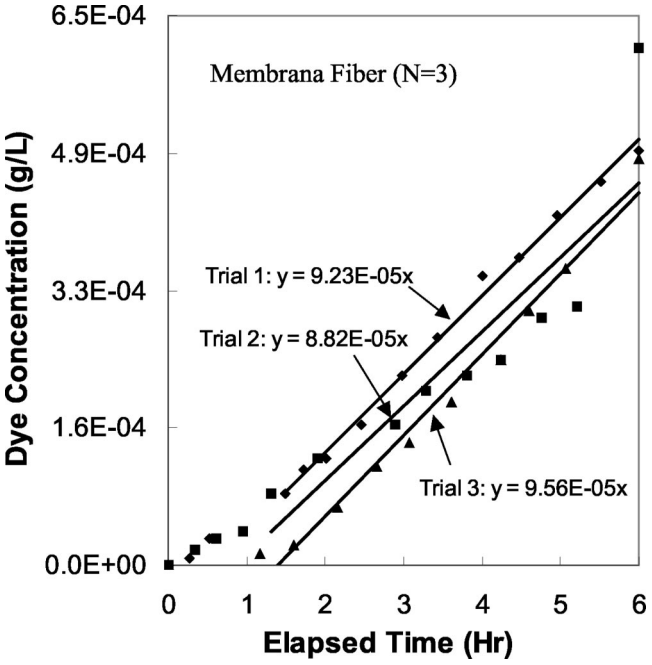

Figure 5. Typical surfactant forced wet-out results for candidate plasma resistant skinned asymmetric fiber, Membrana (n=3).

0.001 were considered to be very highly significant. Differences were considered not statistically significant for $p > 0.05$ but trending toward statistical significance if $0.05 \leq p < 0.10$.

Results

Carbon dioxide and oxygen gas permeance measurements at 23°C and the computed CO_2/O_2 selectivity for all candidate fibers are summarized in **Figure 4**. The highest CO_2 permeance (in ml/s/cm^2/cm Hg) was that for AMT #2453 at 1.71 ± 0.12E-03, followed in descending order by Membrana at 1.40 ± 0.08E-03, AMT #2452 at 1.24 ± 0.05E-03, Senko at 6.79 ± 0.16E-04, and DIC II at 3.15 ± 0.50E-04. The highest O_2 permeance (in ml/s/cm^2/cm Hg) was Membrana at 1.08 ± 0.09E-03, followed by AMT #2453 at 1.03 ± 0.10E-03, Senko at 5.75 ± 1.98E-04, AMT #2452 at 4.37 ± 0.48E-04, and DIC II at 3.40 ± 0.55E-04. In comparison, the nonskinned/composite Celgard ×30–240 fiber had roughly 10- to 100-fold greater gas permeances: 1.62 ± 0.01E-02 ml/s/cm^2/cm Hg for CO_2 and 1.77 ± 0.01E-02 for O_2. CO_2/O_2 selectivity values for the skinned/composite fibers ranged from 2.83 for AMT #2452 to 0.93 for the DIC II fiber.

Gas permeance measurements at 37°C are compared with those at 23°C in **Table 2**. Statistical analysis of each plasma resistant candidate fiber's CO_2 gas permeance did not show any statistically significant differences between 23–37°C results (p-value > 0 .1 for all candidate fibers). O_2 gas permeance statistical analysis for 23°C *versus* 37°C for all candidate fibers also did not show any statistically significant differences (p-value > 0 .1).

Results of a typical fiber wetting study of one skinned asymmetric fiber (Membrana) is shown in **Figure 5** in terms of the increase in dye concentration in the fiber side from bleed through across the fiber wall. Three experiments run under the same conditions are shown, as well as their respective linear slopes (after 1 hour). The nonlinear transients can be seen before 1 hour of testing.

Figure 6 shows the average slope of change in dye concentration *versus* elapsed time (in g/L/hr/m/mm Hg) for all fiber types. DIC II showed the lowest average normalized slope (in g/L/hr/m/mm Hg) of 1.19 ± 0.82E-10 (SA = 0.0079, 0.0085, and 0.0080 m^2), followed in ascending order by Senko at

Table 2. Gas Permeance Measurements at 23°C and 37°C for Plasma Resistant Candidate Fibers

	KO_2 (ml/s/cm^2/cm Hg)		KCO_2 (ml/s/cm^2/cm Hg)	
Name	23°C	37°C	23°C	37°C
Membrana	1.08 ± 0.09E-03	1.07 ± 0.10E-03	1.40 ± 0.08E-03	1.46 ± 0.09E-03
DIC II	3.40 ± 0.55E-04	3.46 ± 0.56E-04	3.15 ± 0.50E-04	2.72 ± 0.24E-04
Senko	5.75 ± 1.98E-04	5.48 ± 1.64E-04	6.79 ± 0.16E-04	5.92 ± 1.24E-04
AMT 2452	4.37 ± 0.48E-04	4.96 ± 0.67E-04	1.24 ± 0.05E-03	1.20 ± 0.09E-03
AMT 2453	1.03 ± 0.10E-03	9.54 ± 2.31E-04	1.71 ± 0.12E-03	1.62 ± 0.21E-03

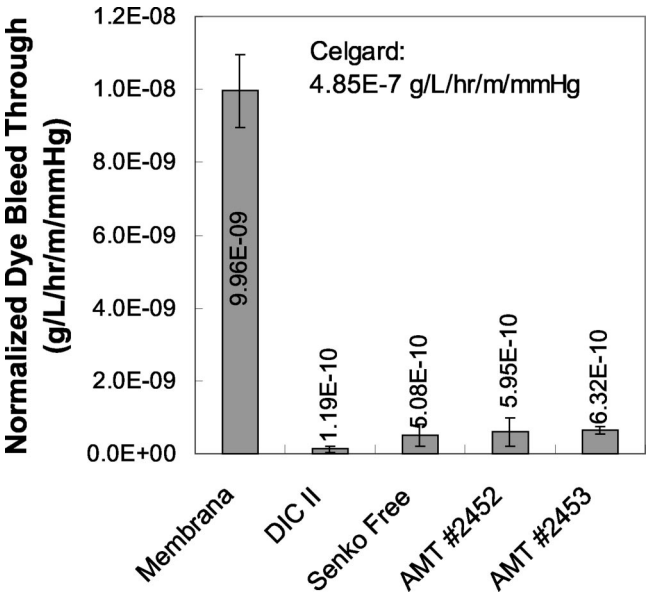

Figure 6. Average Δ Concentration/Δ Time for surfactant forced wet-out tests of candidate plasma resistant fibers (normalized to fiber wall thickness, exposed fiber surface area, and transmural pressure).

5.08 ± 3.13E-10 (SA = 0.0053, 0.0053, and 0.0058 m^2), AMT #2452 at 5.95 ± 4.02E-10 (SA = 0.0057, 0.0055, and 0.0055 m^2), AMT #2453 at 6.32 ± 1.08E-10 (SA = 0.0056, 0.0057, and 0.0056 m^2), and Membrana with the highest slope, at 9.96 ± 1.01E-09 (SA = 0.0087, 0.0086, and 0.0078 m^2). The nonskinned/composite Celgard fibers showed a normalized slope of 4.85E-07 g/L/hr/m/mm Hg (SA = 0.0060 m^2). Membrana showed a highly significant statistical difference between all other candidate plasma resistant fibers (p-value < 0.001). There was a highly significant statistical difference between the DIC II and AMT #2453 fibers (p-value = 0.003). All other plasma resistant fiber comparisons did not show any statistically significant difference (p-value > 0 .1).

Discussion

This study evaluated skinned asymmetric and composite symmetric fibers being developed as "plasma resistant" hollow fiber membranes (HFMs) for artificial lungs. We characterized the "plasma resistance" afforded by the nonporous polymer layers of these HFMs and explored the impact of achieving plasma resistance on the gas permeance of the HFMs. For a given plasma resistant HFM, increasing the thickness and/or continuity of the nonporous polymer layer increases it plasma resistance but always at the expense of a lowered gas permeance. For example, AMT #2452 had a thicker and more continuous siloxane coating than AMT #2453, as is evidenced by its higher CO_2/O_2 selectivity. The CO_2 and O_2 gas permeance values (at 23°C) of AMT #2452, however, were reduced by 28% and 57%, respectively, compared with AMT #2453. The impact of the membrane permeance of a candidate plasma resistant fiber must be considered in the context of its intended application in an artificial lung. Otherwise a rush to select the most plasma resistant HFM might adversely impact gas exchange in the incorporated device.

In artificial lungs, most of the resistance to gas exchange occurs because of diffusion through the liquid (blood) phase and not because of diffusion through the hollow fiber membranes.[10,28,29] Membrane diffusional resistance can become important, however, when skinned or composite HFMs are used in place of standard microporous HFMs.[16] The design objective is to provide sufficient plasma resistance without significantly affecting overall gas exchange because of a low membrane permeance. In what follows, we provide a simple analysis that can be used to estimate the required membrane permeance of a plasma resistant HFM for a given application. An artificial lung's overall permeance (K) is determined by liquid side permeance (K_l) and membrane permeance (K_m) according to

$$\frac{1}{K} = \frac{1}{K_l} + \frac{1}{K_m} \tag{3}$$

where permeance, like a mass transfer coefficient, is an inverse of diffusional resistance and is the gas exchange rate (amount/time) per unit membrane area and per unit partial pressure difference of gas species across each component. The overall permeance of an artificial lung design with standard microporous HFMs (*i.e.,* nonskinned) is given by $K^n \cong K_l$ because membrane resistance is negligible.[10] K for the same artificial lung design with skinned or composite HFMs can be related to that with nonskinned/composite HFMs using $K^{s/c} = \beta K^n$, where β is an acceptable reduction factor in overall gas exchange. Combining the relations yields the required membrane permeance of the plasma resistant HFM:

$$K_m = \frac{K^{s/c}}{1 - \beta} \tag{4}$$

The overall permeance of the artificial lung for each gas (i = CO_2 and O_2) can be estimated from the required gas exchange rate per unit membrane area normalized to the average gas partial pressure difference between blood and sweep gas, that is, $K_i^{s/c} = (\dot{V}_i/A)/\Delta P_i$.

Table 3 shows estimates of the required membrane permeance for artificial lung devices using skinned and composite HFMs. Shown are target K_m values assuming an acceptable 5% and 10% reduction in gas exchange associated with the use of plasma resistant fibers compared with standard fibers. The target K_m values depend upon the gas exchange rate per unit area for the device, shown here based upon use of standard microporous fibers and use of the 5% and 10% K_m fibers in the same device. Comparing **Table 3** with the measured permeances for the candidate plasma resistant fibers (**Figure 4**) indicates that the required O_2 permeance is easily achieved by all candidate fibers. Conversely, the required CO_2 permeance of these fibers is more of a factor depending upon the gas exchange requirements of the artificial lung device. Standard blood oxygenators achieve gas exchange *efficiencies* (here we use the term *efficiency* loosely to refer to the level of exchange expressed on a per unit fiber membrane area) of approximately 50–100 ml/min/m^2, and most of the candidate skinned/composite HFMs have acceptable CO_2 permeances in this range. Some novel artificial lungs under development,[5–9,30–32] however, use active mixing and other strategies to promote more efficient gas exchange, so that smaller implantable or wearable devices can achieve the required O_2 and CO_2 gas exchange

Table 3. Required Membrane Permeance for Artificial Lung Devices using Plasma Resistant Fibers

Device $\dot{V}/A$ (ml/min/m^2)			K_m for Carbon Dioxide (ml/s/cm^2/cm Hg)		K_m for Oxygen (ml/s/cm^2/cm Hg)	
W/uncoated fibers	W/PRFs 5% effect	W/PRFs 10% effect	5% Effect	10% Effect	5% Effect	10% Effect
50	47.5	45	3.33E-04	1.67E-04	2.78E-05	1.39E-05
100	95	90	6.67E-04	3.33E-04	5.56E-05	2.78E-05
200	190	180	1.33E-03	6.67E-04	1.11E-04	5.56E-05
300	285	270	2.00E-03	1.00E-03	1.67E-04	8.33E-05
500	475	450	3.33E-03	1.67E-03	2.78E-04	1.39E-04

Notes: $\dot{V}/A$ shown for a artificial lung device made from uncoated fibers and for the same design made from plasma resistant fibers (PRFs) having a 5% K_m ($\beta = 0.95$) and a 10% K_m ($\beta = 0.90$) value. Computed K_m values assume blood-gas partial pressure differences of 50 mm Hg for CO_2 and 600 mm Hg for O_2.

rates for effective respiratory support. For example, the respiratory support catheter our group is developing[7–10] achieves a gas exchange efficiency of approximately 300 ml/min/m^2. **Table 3** indicates that a CO_2 membrane permeability of 1–2 $\times$ 10^{-3} ml/s/cm^2/cm Hg is required so that the use of skinned/composite fibers in the device reduces overall gas exchange by no more than 5–10% compared with that achieved with standard fibers. Whereas the commercially available Membrana fiber has a CO_2 permeance near the lower end of this range, the custom developed AMT #2453 fiber had a significantly greater CO_2 permeance, near the middle of the desired range, while showing more plasma resistance in our surfactant wetting test. Some artificial lung designs have reported gas exchange efficiencies[32] up to 500 ml/min/m^2, and the membrane permeance requirements may impose a more significant constraint upon these designs.

For simplicity, our standard measurement of gas permeance for plasma resistant fibers is performed at room temperature. Whereas the gas permeance of some of the candidate fibers was different at 37°C compared with room temperature, the differences were not statistically significant (p-value $>$ 0 .1) and do not impact the evaluation of the fibers. The O_2 permeances of all candidate fibers were higher than required for artificial lung devices (**Table 3**). For CO_2 gas permeance, the change with temperature from 23–37°C was small compared with the relatively broad range of 1–2 $\times$ 10^{-3} ml/s/cm^2/cm Hg that we established for our CO_2 permeance target. That permeance was not significantly affected by temperature in this range may be explained by the opposite effects that temperature has upon gas diffusivity and solubility, which are the two (multiplicative) determinants of gas permeability in a polymer.[33]

One issue surrounding coated plasma resistant fibers, like the AMT fibers, is the mechanical stability of the coating. In a separate study, we looked at gas-gas permeance values for AMT coated fibers before and after they underwent a knitting process to create a fiber array. Whereas gas permeance did increase postknitting by approximately 15% and 34%, CO_2 and O_2, respectively, indicating some abrasion and loss of coating, the plasma resistance of the fiber as determined in our surfactant wet out test did not change.

Our study used a surfactant based dye bleed through test to evaluate plasma resistance of the skinned/composite HFMs. A bench test of fiber wet out in human plasma has yet to be successfully developed and would be significantly more difficult, possibly requiring plasma from multiple donors and a longer time frame for evaluation. Comparisons among fibers might be difficult when candidate fibers cannot be tested in the same human plasma. Our measure of "plasma resistance" using the dye bleed through rate in a surfactant forced wet out test is a potentially valid indication of plasma resistance, best used for comparisons among candidate fibers. The kinetics of surfactant (alcohol in our studies) induced wet out are most likely not indicative of plasma induced wet out. Indeed, the surfactant wet out is aggressive, relatively rapid, and may represent a "worse case" evaluation of the candidate HFMs. Dye bleed through in the surfactant test does not necessarily indicate that a fiber is not sufficiently plasma resistant, and even the definition of "sufficient" plasma resistance is likely to depend upon specific applications. A very limited amount of data has been published on ECMO studies using oxygenators made with the Membrana fibers(Quadrox^D, Jostra, Hillingen, Germany, and Hilite 7000LT, Medos, Stolberg, Germany).[22–24] These existing data do not indicate problems of plasma wetting in this application over 6 days, even though the Membrana fiber showed the most dye bleed through in our tests. All of the other candidate skinned/composite HFMs evaluated in this study had lower dye bleed through rates in the surfactant test than the Membrana fiber and by implication may be more plasma resistant than the Membrana fiber. Thus the CO_2 permeance of the various candidate HFMs may be the most important consideration in the overall evaluation of these fibers for artificial lung applications.

Conclusion

We evaluated five different candidate plasma resistant fibers for gas permeance and plasma resistance. All candidate fibers had a sufficiently high oxygen permeance (37°C range of ~3.5E-04 to 1.1E-03 ml/s/cm^2/cm Hg) for typical artificial lung applications. Not all candidate fibers had a sufficiently high carbon dioxide permeance (example: DIC ~2.7E-04 ml/s/cm^2/cm Hg CO_2 permeance at 37°C) for artificial lung applications involving designs with higher gas exchange efficiencies. All candidate fibers had acceptable plasma resistance based upon our forced surfactant wet out test and comparisons with the clinically used Membrana fiber.

Acknowledgment

This study was supported by the US Army Medical Research Development, Acquisition, and Logistics Command under contract No. DAMD17–98–1–8638 and the National Institutes of Health (NIH)

grant No. HL70051. The views, opinions, and findings contained in this report are those of the authors and should not be construed as an official Department of the Army or NIH position, policy, or decision unless so designated by other documentation. The authors thank the University of Pittsburgh's McGowan Institute for Regenerative Medicine for its support.

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