***In Vivo* Measurement of Site-Specific Peritoneal Solute Transport Using a Fiber-Optic-based Fluorescence Photobleaching Technique**

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Fluorescence recovery after photobleaching (FRAP) is a well-established method commonly used to measure the diffusion of fluorescent solutes and biomolecules in living cells or tissues. Here a fiber-optic-based FRAP (*f*-FRAP) system was developed, and validated using macromolecules in water and agarose gels of different concentrations. We applied *f*-FRAP to measure the site-specific diffusion of fluorescein (NaFluo) in peritoneal membranes (PMs) on the liver, cecum, and kidney of a living rat during peritoneal dialysis. Diffusion of fluorescein in PM varied in a time-dependent manner according to the type of organ ($D_{PM \text{ on Liver}}/D_{NaFluo} = 0.199 \pm 0.085$, $D_{PM \text{ on Cecum}}/D_{NaFluo} = 0.292 \pm 0.151$, $D_{PM \text{ on Kidney}}/D_{NaFluo} = 0.218 \pm 0.110$). The proposed method allows direct quantitative measurement of the three-dimensional diffusion in local PM *in vivo*, which was previously inaccessible by peritoneal function test methods such as peritoneal equilibration test (PET) and standardized PM assessment (SPA). *f*-FRAP is promising for local and dynamic assessments of peritoneal pathophysiology and the mass transport properties of PMs, presumed to be affected by variation of tissue structures over different organs and functional changes of the PM with years of peritoneal dialysis.

Keywords : Fluorescence recovery after photobleaching (FRAP), Peritoneal membrane, Diffusion, Fiberoptics
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I. INTRODUCTION

Peritoneal dialysis (PD) is a renal replacement therapy that uses the peritoneal membrane (PM) to remove uremic toxins and excess body fluid from patients suffering chronic

kidney disease. The PM, which covers most intra-abdominal organs and forms the lining of the peritoneal cavity, is a semipermeable membrane with a thickness of about 90 μm and having a large surface area and many capillaries. Numerous researchers have described solute transport in the PM using

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a three-pore model [1]. According to the model, PM consists of different-sized pores, such as water channels (< 0.5 nm), small pores (4 nm), and large pores (> 15 nm), and they are crucial pathways for solute transport through the PM.

The transport properties of the PM not only depend on the individual patient, but also vary over treatment time. Furthermore, structural and functional changes of the PM due to exposure to dialysis solution affect the dynamic behavior of solute transport, and finally result in ultrafiltration failure or peritoneal sclerosis [2]. Therefore, detecting time-dependent functional and structural changes of the PM is important in predicting mass-transfer properties and in characterizing treatment adequacy. However, current methods for testing peritoneal function have difficulty in directly detecting and quantifying peritoneal dysfunction, or can be time-consuming [3]. The simple and most commonly used method, the peritoneal equilibration test (PET), characterizes overall transport, reports qualitative transport properties rather than showing direct mass-transfer parameters, and only gives information for small solutes such as glucose and creatinine. The standardized PM assessment (SPA) was developed to calculate intraperitoneal volume and net transcapillary ultrafiltration [4]. However, SPA analysis procedures are too laborious to analyze dextran using high-performance liquid chromatography. Therefore, currently there is no direct measurement tool to quantify PM function.

Fluorescence recovery after photobleaching (FRAP) is an optical method used to measure the mobility of fluorescent solutes and biomolecules such as proteins and nucleic acids in membranes and aqueous compartments. This method is based on the live-cell imaging technique and can quantitatively analyze diffusive-transport phenomena in a living system [5]. Axelrod *et al.* [6] described the mathematical modeling of FRAP and quantitatively measured the diffusion of biomolecules on a cell membrane. The FRAP technique has been used to measure the diffusion of macromolecules in biological media such as bacterial biofilm [7], articular cartilage [8], and extracellular space of brain and spinal cord in living mice [9]. The FRAP technique can also be applied to tissue-engineering research, because spatial and temporal distributions of growth factor are recognized as crucial factors in controlling the differentiation and growth of specific types of cells [10].

In this study we developed a fiber-optic-based FRAP (*f*-FRAP) apparatus to measure site-specific and time-dependent diffusion of fluorescent solutes in the PM of a living rat, which is not accessible by conventional testing methods. In contrast to existing optical techniques with limited penetration depth of light, light can be delivered through a flexible optical fiber with a micron-sized tip to the deep, confined parts in living mice for FRAP measurements, as demonstrated in previous studies [11, 12]. The proposed *f*-FRAP method was validated using *in vitro* tests with solutions and agarose gels mixed with fluorescein or fluorescein dextrans, and applied to the measurement of dynamic diffusion rates of solutes in the PMs on the liver, cecum, and kidney of rats during PD.

II. MATERIALS AND METHODS

2.1. Theory of FRAP

In the FRAP technique, the fluorescence-recovery signals within the bleached region are recorded as a function of time (see Fig. 1(a)). For a Gaussian beam, fluorescence recovery is described as follows [13, 14]:

$$F(t) = \left\{ F^0 \sum_{n=1}^{\infty} \frac{(-K)^n}{n!} \frac{1}{1 + n(1 + 2(t/\tau)^\alpha)} \right\} R + (1 - R)F(0) \quad (1)$$

$$R = \frac{F(\infty) - F(0)}{F^0 - F(0)} \quad (2)$$

where F^0 is the fluorescence intensity before photobleaching, $F(0)$ represents the fluorescence intensity immediately after photobleaching, $F(\infty)$ is the fluorescence intensity at the time when recovery is complete, K is a parameter related to bleaching depth, α is a parameter describing the motion of molecules ($\alpha = 1$ for free diffusion and $\alpha < 1$ for anomalous diffusion), R is the mobile fraction, and $\tau = w^2/4D$ is the characteristic diffusion time [6, 9, 15], where w is the radius of the laser beam and D is the diffusion coefficient.

Equation 1 can be simplified as follows [12]:

$$F(t) = \frac{F(0) + (R(F^0 - F(0)) + F(0))\left(\frac{t}{t_{1/2}}\right)^\alpha}{1 + \left(\frac{t}{t_{1/2}}\right)^\alpha} \quad (3)$$

$$t_{1/2} = \beta\tau = \frac{\beta w^2}{4D} \quad (4)$$

where $t_{1/2}$ is the time at which the fluorescence intensity has recovered by 50%, α is a parameter describing the motion of molecules, and β is a parameter related to the fraction of bleaching and the effective bleached spot size.

From the fluorescence-recovery signals we obtained the fractional fluorescence recovery curve using the following relation:

$$f(t) = \frac{F(t) - F(0)}{F(\infty) - F(0)} \quad (5)$$

The fractional fluorescence-recovery curve can be fitted using

$$f(t) = \frac{R(t/t_{1/2})^\alpha}{1 + (t/t_{1/2})^\alpha} \quad (6)$$

where α is a time exponent ($\alpha = 1$ for free diffusion and $\alpha < 1$ for anomalous diffusion, as above).

FIG. 1. (a) Principle of fiber-optic-based fluorescence recovery after photobleaching (*f*-FRAP). (b) Schematic diagram of *f*-FRAP setup. (c) Photo of optical-fiber tip (bar = 200 μ m). (d) 3D reconstructed plot (left image shows a quarter of axisymmetric beam shape) and 3D contour plots (right image) of volume-illuminated beam profile measured around the fiber tip (bar = 50 μ m).

In the *f*-FRAP system the excitation-beam profile varies according to the size and shape of the optical fiber's tip. We therefore deduced the relative diffusion coefficients using the following relation, as in a previous study [11]:

$$D_r = \frac{D_{\text{sample}}}{D_{\text{solution}}} = \frac{t_{1/2}(\text{solution})}{t_{1/2}(\text{sample})} \quad (7)$$

Measured diffusion coefficients of fluorescent solutes in samples (D_{sample}) were normalized by those in water (D_{solution}) using the same optical-fiber tip.

2.2. Instrumentation

A diagram of the *f*-FRAP system is shown in Fig. 1(b). A continuous-wave blue diode laser (MBL-III-473-100MW, Changchun New Industries Optoelectronics Tech., China) was used for illumination. A laser beam of wavelength 473 nm was reflected by a dichroic mirror (Di01-R488-25 $\times$ 36, Semrock, USA), focused onto the back of a multimode optical fiber by an objective (10 $\times$ /0.25NA; NT36-132, Edmund Optics, USA), and delivered to the sample. As shown in

Fig. 1(c), custom-made optical fibers (0.5 m long and 50 μ m diameter core, OZ Optics, Canada) with 8 $^\circ$ tapered tips coated in aluminum at the distal end were used to enhance the efficiency of the light transmission [11]. Subsequently, 521-nm fluorescence from the sample passed through the fiber, objective lens, dichroic mirror, a mechanical shutter (VS35S2T1, Vincent Associates, USA), and an emission filter (FF01-530/43-25, Semrock, USA) before reaching the photomultiplier tube (H9306-04, Hamamatsu, Japan). We used a neutral density filter (NE30B, Thorlabs, USA) mounted on a motorized flipper (MFF001/M, Thorlabs, USA) to control the output intensity of the laser beam for illumination. The flipper position was toggled by a 5-V external trigger signal and synchronized with the mechanical shutter, which was equipped to block the photomultiplier tube detector from a high-intensity laser pulse. Prior to the bleaching pulse, initial fluorescence data were sampled at a rate of 100 Hz continuously for 700 ms with a laser intensity of 0.01-0.1 mW, reduced by the neutral density filter. After photobleaching the sample at a laser power of 20-30 mW for a short period of time ($\sim$ 500 ms), the fluorescence-recovery signal was detected by the lower-intensity laser until the

signal reached a plateau. Data were collected for 58.22 s and 38.21 s after photobleaching in *in vitro* and *in vivo* experiments, respectively. The overall system was controlled by a program we developed using LabVIEW software (National Instruments, USA), and the data were automatically saved in a computer using a data acquisition (DAQ) board (USB-6251 BNC, National Instruments, USA).

2.3. Instrument Validation

We measured the beam profile of the volume illumination generated by the tapered optical fiber using a laser-beam profiler (SP620U, Ophir Optronics Solutions Ltd, Israel) at 100 cross sections spaced with an interval of 10 μm from the fiber tip. To prevent saturation of the laser-beam intensity, neutral density filters (NE10B, NE20B and NE30B, Thorlabs, USA) were aligned in front of the laser, reducing the intensity by a factor of 10^{-6} . The laser-beam profile emitted from the fiber tip is displayed in Fig. 1(d), which shows the actual excitation field in our photobleaching experiments. To validate the proposed *f*-FRAP system, relative diffusion coefficients (D/D_0) were measured using solutions of fluorescein sodium salt (NaFluo; 376 Da, excitation peak = 460 nm, emission peak = 515 nm, F6377; Sigma-Aldrich, USA) and fluorescein dextrans (3, 10, and 70 kDa, excitation peak = 494 nm, emission peak = 521 nm; Invitrogen, USA) to investigate the effects of the molecular weights of molecules on relative diffusion coefficients. The Stokes-Einstein equation was used to compare the theoretical and experimental values of D/D_0 for fluorescein dextran solutions:

$$\frac{D}{D_0} = \frac{\frac{k_B T}{6\pi\eta r}}{\frac{k_B T}{6\pi\eta r_0}} = \frac{r_0}{r} = \frac{(MW_0)^{1/3}}{(MW)^{1/3}} \quad (8)$$

where D is the diffusion coefficient, k_B is Boltzmann's constant (1.38×10^{-23} J/K), η is the viscosity, T is the absolute temperature, r is the radius of the molecule, and MW is the molecular weight. Equation 8 assumes that viscosity and

absolute temperature are constant, and that the density of the molecule is negligible.

To determine the feasibility of the proposed technique for investigating tissue structure of the PM, relative diffusion coefficients were also measured using different concentrations (0.5, 2.5, and 4.5%) of agarose gels mixed with NaFluo or fluorescein dextrans (3 and 10 kDa). The concentrations of both NaFluo and fluorescein dextrans were 4 mg/ml. We hypothesized that the pore size of the agarose gel would affect the diffusion of molecules. The concentration of agarose was controlled to make different pore sizes of agarose gel. The pore size of 0.5% gel has been reported to be 450 nm [16]. All measured diffusion coefficients were normalized with respect to the diffusion coefficient of NaFluo in solution using the same optical-fiber tip to correct the geometrical variation of the illumination volume at the tip of the fiber.

2.4. Animal Experiments

The local ethical committee for animal experiments approved the experimental protocol used in this study (IACUC No. 10-0174). The feasibility of using NaFluo as a surrogate marker for low-molecular-weight solutes in the PM was evaluated using the PET for 2 h with 6-week Sprague-Dawley rats ($n = 4$ or 5). After placing a catheter in the peritoneal cavity of the rat, PD was carried out with 2.5% dextrose solution for 3 to 7 days. During the PD, dialysate was sampled from the peritoneal cavity of the rat at 0, 30, 60, 90 and 120 min. The dialysate samples were analyzed using spectroscopy and a glucometer, and concentrations of glucose and NaFluo were compared.

To measure the site-specific diffusion in the PM, the rat was anesthetized on a heating plate to maintain the temperature of the body, dialysate mixed with NaFluo (60 mg/ml) was injected into the tail vein, and dialysate was infused into the peritoneal cavity (see Fig. 2(a)). One minute after the injection, the rat's abdomen was opened and we replaced the dialysate with fresh solution in the peritoneal cavity to maintain the initial condition. Then the optical-fiber tip was placed on the surface of the local PM that covers an

(a)

(b)

FIG. 2. (a) Schematic of *f*-FRAP measurement on the PM of the rat. The figure in the right box shows the 3-pore model used to describe solute transport in the PM. (b) Laser-beam spot from the optical-fiber tip placed on the PM of the rat.

organ (liver, kidney, or cecum), as shown in Fig. 2(b). We tried not to penetrate the PM with the fiber tip because NaFluo molecules diffuse from the capillaries distributed in the PM to the peritoneal cavity. Thus, if we insert the fiber tip deep into the tissue beyond the PM, we cannot obtain fluorescent signals. After confirming the initial fluorescence signals, the diffusion of NaFluo in the PM was measured. We obtained the relative diffusion coefficients of NaFluo in the PM of the rat from each fluorescence-recovery curve and calculated the averaged values of the diffusion coefficients. When we calculated relative diffusion coefficients of NaFluo on each organ, we averaged whole diffusion coefficients regardless of time. Also, when we calculated relative diffusion coefficients of NaFluo at different time periods, we sorted the relative diffusion coefficients according to the time interval (1-15, 16-30, 31-45 and 46-60 min), and calculated averaged values for each period of time.

We repeated the measurement 3-10 times using two rats during the PD (1-15, 16-30, 31-45 and 46-60 min) on the liver, the cecum, and the kidney. In every measurement, we selected different spots on the PM of each organ to avoid excessive photobleaching of NaFluo, and the elapsed time was recorded immediately after injection of dialysate mixed with NaFluo into the tail vein. To observe site-specific dynamic mass transport in the local PMs, we calculated both time-dependent and time-averaged diffusion.

2.5. Data Analysis

Time-series data were obtained from the photomultiplier tube to calculate the fractional intensity. Our in-house program collected the data before and after photobleaching of the sample. In the *in vitro* study we used 3-5 sets of data to calculate the half-time recovery ($t_{1/2}$) and D/D_0 using Eqs. 6 and 7. Then, under *in vivo* conditions, we obtained 3-9 sets of data, which were used to deduce D/D_0 .

III. RESULTS

Our *in vitro* test showed that D/D_0 decreased as the molecular weight of dextran increased (see Table 1). Measured D/D_0 showed good agreement with theoretical values for fluorescein dextrans with molecular weights of 3, 10, and 70 kDa. The absolute diffusion coefficients can be calculated based

on the diffusion coefficient of the base solution. As shown in Fig. 3, diffusion is faster in agarose gels with larger pore size, and for molecules that have lower molecular weights. Significantly different values of D/D_0 were observed among NaFluo and 3-kDa and 10-kDa fluorescein dextrans ($p < 0.001$). D/D_0 of solutes decreased by 77% (NaFluo, 0.5% gel), 85% (NaFluo, 2.5% gel), 89% (NaFluo, 4.5% gel), 89% (3-kDa dextran, 0.5% gel), 93% (3-kDa dextran, 2.5% gel), 93% (3-kDa dextran, 4.5% gel), 93% (10-kDa dextran, 0.5% gel), 95% (10-kDa dextran, 2.5% gel), and 96% (10-kDa dextran, 4.5% gel).

NaFluo and glucose showed similar kinetic behavior in the peritoneum of the rat. Figure 4(a) shows normalized solute concentration profiles for NaFluo and glucose during the PET. Figure 4(b) shows concentration profiles with time in logarithmic scale between 30 and 120 min. The slopes of the fitted lines for NaFluo (8 mg/ml), NaFluo (2 mg/ml), and glucose were -0.454, -0.445, and -0.650 respectively. Even though the slope of glucose was higher than those of

FIG. 3. Comparison of relative diffusion coefficients D/D_0 in agarose gels. There were significant differences among NaFluo and 3-kDa and 10-kDa dextrans ($p < 0.001$).

TABLE 1. Comparison of experimental and theoretical relative diffusion coefficients D/D_0 in solution

Sample (MW)	D/D_0 (experimental)	D/D_0 (theoretical)	$D (\times 10^{-6} \text{ cm}^2/\text{s})$ (absolute)
NaFluo (376 Da)	1	1	4.20 ^a
Fluo-dextran (3 kDa)	0.70±0.160	0.50	2.95
Fluo-dextran (10 kDa)	0.39±0.190	0.34	1.64
Fluo-dextran (70 kDa)	0.18±0.042	0.18	0.77

^a Casalini *et al.* (2011) [28]

NaFluo, the three curves showed linear and consistent profiles during the PET. Therefore, NaFluo was applied as a surrogate marker to track relative mass transfer in the PM.

Based on animal experiments, we observed site-specific and time-dependent diffusion of NaFluo. Averaged relative diffusion coefficients of NaFluo in PM on each organ of the rat are listed in Table 2. The local PMs covering the cecum showed a higher D/D_0 , whereas the lowest D/D_0 was

FIG. 4. (a) Concentrations of NaFluo and glucose during PET. (b) Concentration profiles of solutes with time in logarithmic scale.

TABLE 2. Comparison of relative diffusion coefficients D/D_0 of NaFluo in peritoneal membrane on each organ of the rat

Sample	Relative diffusion coefficient (D/D_0)
NaFluo solution	1
PM on Liver	0.199 ± 0.085
PM on Cecum	0.292 ± 0.151
PM on Kidney	0.218 ± 0.110

observed in the PM covering the liver. Figure 5 shows the averaged fractional fluorescence-recovery curves obtained for cecum. Figure 6 describes the time-dependent diffusion

FIG. 5. Fractional fluorescence-recovery curves obtained in cecum.

FIG. 6. Relative diffusion coefficients D/D_0 of NaFluo in peritoneal membrane at different time periods: (a) cecum, (b) kidney.

behaviors in the PMs covering the cecum and the kidney. Data for the liver were not displayed because the fluorescence signal was too weak to detect at the initial phase (1-15 min). D/D_0 of the PM covering the cecum decreased with time, whereas that of PM covering the kidney increased.

IV. DISCUSSION

In this study we developed the f -FRAP system to measure the transmembrane diffusion of solutes at the PM of the rat. We validated the device using *in vitro* experiments, and it showed reliable performance in the measurement of diffusion coefficients. We applied the f -FRAP to direct measurement of mass transport in the PMs of rats. Our method allowed direct measurement of the diffusion in the local PM, and showed site-specific and time-dependent behaviors during PD.

Solute transport in the PM is related to the mass transfer coefficient (MTC) and the mass transfer area coefficient (MTAC) across the PM (Eqs. 9 and 10) [17]. The MTAC of the whole PM is the same as the sum of the products of the MTC and the surface areas of the specific tissues immersed in the dialysate:

$$MTC = \sqrt{D(pa)} \quad (9)$$

$$MTAC = \sum_{i=1}^n MTC_i A_i \quad (10)$$

where (pa) is the capillary permeability-area product and A_i is the area of the specific tissue. Diffusion rates in the PM vary with time during PD because ultrafiltration and diffusion occur in the early stage of PD, while reabsorption occurs in the later stage [18, 19]. Furthermore, the transport properties of the PM change with time during PD due to peritonitis, ultrafiltration failure, and peritoneal sclerosis [20]. For example, sclerosis or adhesion decreases solute transport by thickening of the PM or reduction in surface area, while angiogenesis or peritonitis increases solute transport by enhancement of capillary perfusion [21].

The most common cause of ineffective fluid removal in PD is loss of ultrafiltration capacity due to increased solute transport (high transporters). Impaired ultrafiltration severe enough to require cessation of PD occurs in about 10% of cases [22], which then requires referral to alternative renal-replacement therapy. Long-term PD for more than 2 years, repeated peritonitis, exposure to glucose in PD solution, diabetes, and beta-blockers contribute to these phenomena [23, 24]. Therefore, detecting time-dependent functional and structural changes of the PM is important to sustain PM function in the long term, and to plan any referral to alternative renal-replacement therapy. Currently, test methods monitoring PM function, including PET, provide indirect estimation based on time-averaged dialysate properties. These

methods are not able to provide direct information about pathological properties of PM. The mechanism for transport of mid-sized molecules in peritoneal dialysis seems to be a combination of size-selective diffusion and convection through large pores of the PM. However, this hypothesis is still under debate due to lack of a direct measurement tool.

An f -FRAP system can measure absolute diffusion coefficients and convection of solutes directly during PD, which can be a useful tool for analysis of peritoneal transport in combination with the tests of PM function currently used. First, in an animal model of peritoneal membrane dysfunction such as encapsulating peritoneal sclerosis, f -FRAP is able to measure site-specific transport properties of PM before and after peritoneal dysfunction. Second, transport mechanisms of solutes in PM are related to various pathological changes in PM. Ultrafiltration failure, inflammation, and sclerosis can be quantitative diagnoses of PM function. Finally, if an f -FRAP system is developed as a minimally invasive PD catheter technique, it can be used to predict quantitative PM function, making it possible to monitor the progression of PM function with time. In each step of progression, a patient-specific PD solution can be selected based on this information, which provides new biocompatible PD solution development.

In this study we selected NaFluo as a surrogate biomarker for glucose. Ideally, fluorescent glucose analogues should be used for such a study, but they were not available at that time, to our knowledge. Although there is a difference in absolute value for glucose, due to greater molecular weight and negative electrical charge, NaFluo mimicked the overall kinetic behavior of glucose (see Figure 4). Therefore, NaFluo was useful as a surrogate biomarker for small-solute transport in the PM. Different parts of the peritoneal barrier may have different transport characteristics. The permeability, distribution, and surface area of the capillaries within different parts of the PM may have an impact on overall fluid and solute transport [25]. Our results are in good agreement with those of Flessner [17], who measured small-solute transport across a specific PM in a rat. Flessner [17] also measured the MTC of both peritoneal-cavity-to-plasma and plasma-to-peritoneal-cavity transport, and found that the MTC values in both directions were nearly the same. This result suggests that our experimental method to measure the diffusion of NaFluo from a capillary to the peritoneal cavity is valid. Therefore, we were able to measure diffusion coefficients in different sites of the PM at different time points. While D/D_0 of NaFluo in the PM on the cecum decreased slightly, that on the kidney sharply increased over time.

Different local diffusion coefficients might be related to the microvasculature of the PM and local microcirculation. Gotloib *et al.* [26] showed the heterogeneous density and ultrastructure of peritoneal microvasculature using electron microscopy. In their study, the mesentery appeared as the most vascularized peritoneal segment (71.1% of the total number of observed capillaries). Diaphragmatic and parietal peritoneum contributions to the total examined microvascular bed were

17.9% and 10.9%, respectively. Ronco [27] suggested a “nearest capillary” hypothesis to explain the impact of peritoneal blood flow and microcirculation on dialysis efficiency. Considering the peritoneal microvasculature as a network of capillaries with a three-dimensional distribution and different distances from the mesothelium, the solute diffusion distances and the glucose back-diffusion distances may be different for different populations of capillaries. Time-dependent diffusion behaviors are difficult to interpret with our current knowledge. However, these peritoneal transport properties might be related to tissue perfusion. When cardiac output decreases during anesthesia, blood perfusion into vital organs such as the kidney is sustained, while peripheral perfusion decreases.

V. CONCLUSION

We designed an *f*-FRAP system to study transport phenomena in the PM of a rat *in vivo*. We found that the diffusion characteristics of the PM vary according to both the positions of the PM and time. A future study will examine solute transport characteristics in normal and abnormal PMs. Both diffusion and ultrafiltration in the PM can be measured using an optical-fiber tip with axis perpendicular to the flow direction, combined with fluorescent makers with large molecular weights. The proposed method can be used to assess morphological and functional effects in the PM with respect to PD solutions or drugs, in combination with PET and SPA. Future work with fluorescent glucose analogues can provide more precise insight into peritoneal transport, specifically, in an animal model of peritonitis and peritoneal sclerosis.

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