Development of Vascular Tissue Polyvinyl Alcohol Surrogates with Adjustable Diffusional Properties

Rosaire Mongrain, Toufic Jrab, Hubert Laflamme, Karim Mustafa
Department of Mechanical Engineering, McGill University, Monreal, Canada
Email: rosaire.mongrain@mcgill.ca

Summary

Molecular compounds and nanovesicles are increasingly used with drug eluting stent (DES). The numerical modeling of DES concentration distribution is a very useful method to investigate and optimize the DES design characteristics (coating thickness, strut dimensions, diffusion coefficient). However, the verification of these numerical models remains a challenge because of the difficulty to access human vascular tissue and assess the compound concentration in the tissue. A method to fabricate surrogate vascular tissue with adjustable diffusional properties is presented.

Introduction

Drug eluting stents are used to inhibit neointima growth after stent implantation using anti-proliferative compounds. An objective is to ensure efficient treatment with homogeneous drug concentration distribution in the wall [1]. PVA hydrogels can be used as phantom material for diffusional models to study DES compound dispersion [2]. A synthesis method using graphene oxide (GO) is described to modify the PVA porosity to adjust the diffusion coefficient. Briefly, we present methodologies to synthesize thin hydrogel surrogate membranes, assess the impact of the GO additive on the porosity and measure the diffusion coefficient.

Methods

We developed a protocol to fabricate Poly Vinyl Alcohol (PVA) vascular tissue surrogate [3]. The mechanical properties can be modified because PVA crystallinity changes during freezing/thawing cycles [3]. Briefly, a PVA solution (P1763, Sigma) in 10%wt deionised water is prepared and freezed/thawed with a Peltier plate (IC25XT, Torrey Pines). A ramp temperature of 0.33˚C to -20˚C for 2 hours is followed by thawing at a 0.08˚C ramp to 10˚C for 2 hours.

Graphene Oxide (GO) was shown to affect water penetration in hydrogels as it can modulate the porosity [6]. Thin PVA surrogates were then prepared with and without GO and the resulting effective diffusion coefficients were measured using a customized Franz cell. The cell has two compartments, one with a known concentration of a compound (donor) and one with an initial zero concentration (receptor). The cell compartments are filled with distilled water and brought to 40°C. Initial tests were done with 1.5 mL of methyl blue poured into donor chamber. Triplicate samples were collected every 5 minutes for one hour and their absorbance was measured with spectroscopy at 664 nm. The Diffusion coefficient is estimated with $D = \frac{1}{\beta t} ln\left(\frac{c_{i,donor} - c_{i,receptor}}{c_{f,donor} - f}\right)$, with c_i, c_f, are the initial and final concentrations and β a calibration constant [4].

Results and Discussion

PVA hydrogel surrogates were prepared with thicknesses of 200-500 µm (Fig 1a) with and without GO and imaged with SEM (Fig 1b, c). We note the impact of GO on the porosity. The Franz cell results are plotted as a function of time (Fig 1d). The estimated diffusion coefficient is $D=2.91\times10^{-10}$ m^2/s, which is close to the value for skin $(2.2\pm0.9)\times10^{-10}$ m^2/s [5].

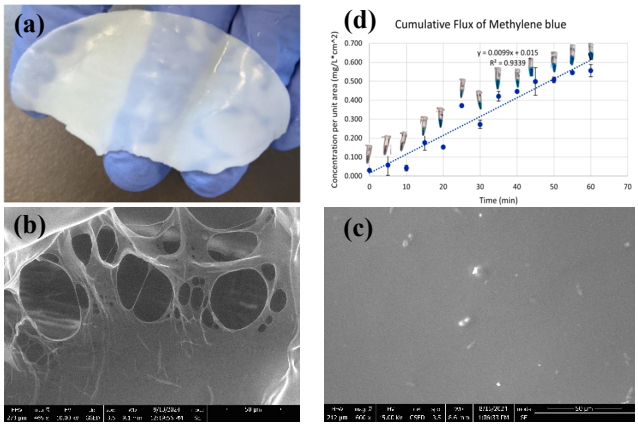

Figure 1: a) Thin PVA surrogate, b) standard PVA porosity (10% PVA), c) PVA+GO porosity (10% PVA + 1% GO) and d) Franz cell diffusion tests with methyl-blue and standard PVA

Conclusions

The results show that the PVA surrogate membranes have the potential to mimic vascular tissue diffusional properties. This would provide a tool to standardize the assessment of molecular compounds under controlled and reproducible conditions and explore different values of diffusion coefficients by adjusting the PVA surrogate porosity with the GO additive.

Acknowledgments

The authors gratefully acknowledge funding from the Natural Sciences and Engineering Research Council of Canada.

References

[1] Mongrain et al, *J Biomech Eng*, **129**(5):733-42, 2007
[2] Abbasnezhad N et al., *Polymers*, **14**(13), 2751
[3] Pazos V, *J Mech Behav Biomed Mater* **2**(5):542-49, 2009
[4] Cussler E, *Diffusion: mass transfer in fluid systems,* 2009
[5] Genina, A et al., *Medic Laser Applic*, **23**(1): 31-38, 2008
[6] Morimune et al., *Polymer Journal* **44** :1056–1063, 2012