

# PERFORMANCE EVALUATION OF TISSUE ENGINEERING SCAFFOLDS - DEVELOPMENT OF A NOVEL TOOL FOR OPTIMIZATION OF FLUID FLOW & PERMEABILITY

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## INTRODUCTION

Fabrication of three-dimensional, biodegradable scaffolds has become an increasingly important tissue engineering approach for bridging of massive tissue defects. Scaffolds are designed to provide a mechanically and biochemically controlled microcosm for cell seeding or ingrowth, matrix formation, and tissue regeneration [5] within the prevailing tissue environment where they are implanted. In particular, their mechano-chemo-biological interactions with their environment may be exploited to enhance cell migration and proliferation as well as to promote molecular and fluid transport [3,4].

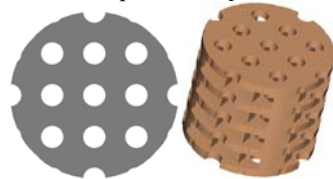
Tissue engineering scaffolds are manufactured using a variety of techniques and materials. Rapid prototyping (RP) techniques have proven to be particularly beneficial in tissue engineering, as they offer advantages including ease of manufacture, control of macrostructure to fit a specific geometry, as well as a well-defined microstructure that can be optimized for site-specific applications [2]. Resolution of microstructure is critical for optimization of fluid transport and permeability in scaffolds; the latter, in turn, influence cell viability throughout the volume of tissue that is to be regenerated [3]. Yet, the degree to which rapid prototyped designs meet technical specifications is unknown. On the one hand, discrepancies between the desired and manufactured structure are technically unavoidable due to viscosity of the lithography resin and surface tension effects as well as laser spot resolution. On the other hand, such discrepancies may influence directly the functionality, and hence the success, of tissue engineering scaffolds.

To date, no design tool is available to optimize porosity and permeability of scaffolds for specific geometries. The goal of this study is to develop such a tool that could i) aid in optimizing design prior to empiric testing of scaffolds (*e.g. in vivo*) and ii) provide a platform to investigate the effect of deviation from design specifications on performance functions including fluid flow and permeability. First, we implemented a  $\mu$ CT-imaging based approach to determine how closely rapid prototyped scaffolds met design specifications. Then we used a computational fluid dynamics approach to calculate permeability of the target (CAD-based measurements) and

actual ( $\mu$ CT-based measurements) scaffold geometries. Finally, we measured scaffold permeability experimentally to validate the computational predictions.

## MATERIALS AND METHODS

Scaffolds, comprising a three-dimensional layered cylinder with nine circular and four semi-circular channels in the longitudinal direction (Fig. 1), were created using a solid modeling program (Pro/Engineer, PTC) and then fabricated using stereolithography (SLA), a rapid prototyping technique ( $n = 7$ ). Four rapid prototyped scaffolds were imaged using  $\mu$ CT (Scanco, Bassersdorf, CH), whereby 700 slices were imaged at a resolution of 12  $\mu$ m. The remaining three scaffolds were used for the experimental permeability measurements.



**Figure 1. Theoretical scaffold geometry with thru-channels in longitudinal direction (length = 5.2 mm, radius = 3 mm, thru-channel dia. = 0.4 mm).**

To predict flow through the target design scaffold and through actual rapid prototyped scaffolds, a fluid mesh was created and fluid flow was calculated using a computational fluid dynamics software package (CFD-ACE, CFDRC, Huntsville, AL). Variance between the target and actual geometries was modeled by reducing iteratively (0-100%, in 25% increments) the thru-channel diameters in the scaffold. Flow was induced via a pressure gradient, for a fluid medium idealized as water (density = 1000 kg/m<sup>3</sup>, viscosity = 0.001 kg/ms). Based on the mass flow rate calculated through the fluid mesh of each computational scaffold, permeability was determined using Darcy's

Law (Eq. 1)

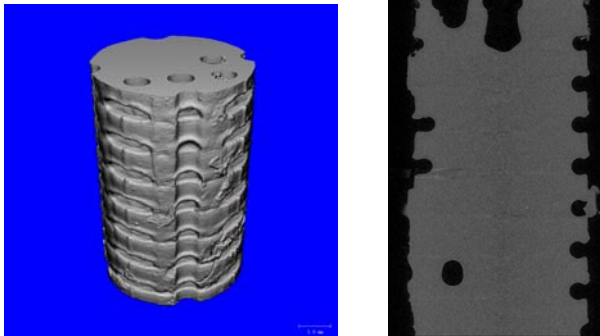
$$k = \frac{\dot{m} \mu L}{A_{cs} \rho \Delta P} \quad (1)$$

where  $k$  is permeability ( $m^2$ ),  $\dot{m}$  is mass flow rate,  $\mu$  is fluid viscosity,  $L$  is scaffold length,  $A_{cs}$  is cross-sectional area,  $\rho$  is fluid density, and  $\Delta P$  is the applied pressure gradient. Permeability in the longitudinal direction was calculated according to (1) and validated experimentally in the laboratory using the same mass flow rate.

## RESULTS

Reducing thru-channel diameter has a dramatic effect on scaffold permeability. Based on actual rapid, rapid prototyped scaffold measurements, variance between actual and target scaffold geometries can reduce permeability to below the desired value for successful tissue ingrowth. Using the flow simulations and the calculated permeability for the scaffolds of decreasing thru-channel dimension, an equation was generated to predict the permeability of physical scaffolds based on their thru-channel dimension, as this was the most critical dimension to flow (Fig. 2, equation at top of plot).

Experimental measurement of scaffold permeability based on Darcy's Law has been limited due to the limitations of the manufacturing method used; to date, thru-channels have not connected through the structure or rapid prototyped scaffolds and thus have drastically limited their permeability. This finding was corroborated by  $\mu$ -CT scans (Fig. 3) which allowed for precise measurement of deviation from specifications.



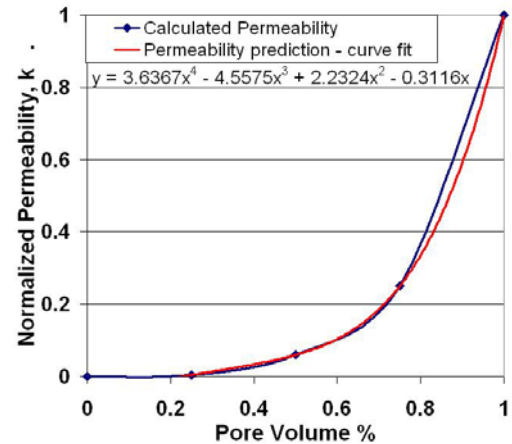
**Figure 3. Micro-CT images of impermeable scaffold created using SLA: (a) full structure, (b) center cross-section**

## DISCUSSION

This study introduces a novel tool to predict and optimize scaffold performance parameters, including fluid flow and permeability, prior to scaffold manufacture. Whereas tissue engineering scaffolds provide a means to promote cell growth, matrix formulation, and tissue regeneration, fluid flow and permeability are critical to promote cell viability and proliferation, as well as tissue development [3-5], within the scaffold structure. This study implemented predictive computational fluid dynamics models and experimental measures to evaluate and validate variance in dimensions and permeability between target and actual scaffold geometries. The computational model provided a platform to calculate permeability for a range of channel diameters simulating a range of prototyping discrepancies between target and actual geometry. This data allowed us to develop a predictive equation for scaffold permeability based on the approximate actual thru-channel dimension compared to target dimension.

Interestingly, seven rapid prototyped SLA scaffolds were shown to be impermeable based on  $\mu$ CT and experimental measurements; this was due to lack of continuity in the scaffold thru-channels. Had we had our predictive model and equation prior to rapid prototyping of the pilot scaffolds, we could have optimized our design for function prior to the prototyping phase.

Limitations in this study include the small sample size as well as the type of scaffolds available for measurement. The computational model presented here is applicable for the specific scaffold design that was available for study; other scaffold types will be modeled and validated to create a more robust platform for scaffold performance prediction and evaluation.



**Figure 2. Calculated permeability (normalized to desired) for computational scaffolds with decreasing thru-channel dimension (% of desired diameter)**

Overall, this study sought to determine the impact of differences between target and actual geometries on tissue engineering scaffold permeability. It was found that for this scaffold design, permeability could be predicted from thru-channel dimension. Thus, for rapid prototyped scaffolds, thru-channel measurements can yield a quick estimate of the resultant permeability for the structure, where scaffolds below the desired level of permeability required for the specific application can be discarded.

This study presents, for the first time to our knowledge, a novel design tool to investigate the effect of differences, between design specifications and actual manufactured geometries, on fluid flow and permeability. Furthermore, it provides a platform to predict and optimize porosity and permeability of scaffolds for specific geometries, thus reducing the number of experimental studies necessary to validate design performance.

## REFERENCES

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