JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 34 (2014) 253–263

Available online at www.sciencedirect.com

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Research Paper

Comparison of the direct burst pressure and the ring tensile test methods for mechanical characterization of tissue-engineered vascular substitutes

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ARTICLE INFO

Article history:
Received 8 October 2013
Received in revised form
10 February 2014
Accepted 13 February 2014
Available online 21 February 2014

Keywords:
Burst pressure
Ring tensile test
Tissue engineering
Vascular substitutes
Mechanical properties
Laplace's law

ABSTRACT

Tissue engineering provides a promising alternative for small diameter vascular grafts, especially with the self-assembly method. It is crucial that these grafts possess mechanical properties that allow them to withstand physiological flow and pressure without being damaged. Therefore, an accurate assessment of their mechanical properties, especially the burst pressure, is essential prior to clinical release. In this study, the burst pressure of self-assembled tissue-engineered vascular substitutes was first measured by the direct method, which consists in pressurizing the construct with fluid until tissue failure. It was then compared to the burst pressure estimated by Laplace's law using data from a ring tensile test. The major advantage of this last method is that it requires a significantly smaller tissue sample. However, it has been reported as overestimating the burst pressure compared to a direct measurement. In the present report, it was found that an accurate estimation of the burst pressure may be obtained from a ring tensile test when failure internal diameter is used as the diameter parameter in Laplace's law. Overestimation occurs with the method previously reported, i.e. when the unloaded internal diameter is used for calculations. The estimation of other mechanical properties was also investigated. It was demonstrated that data from a ring tensile test provide an accurate estimate of the failure strain and the stiffness of the constructs when compared to measurements with the direct method.

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http://dx.doi.org/10.1016/j.jmbbm.2014.02.017
1751-6161

1. Introduction

The prevalence of cardiovascular diseases has led to the necessity of obtaining suitable small diameter vascular substitutes through the development of substitutes by tissue engineering. Currently, the gold standard for treatment of coronary or peripheral vascular diseases is the replacement of the damaged blood vessels using a segment of the patient's internal mammary artery or saphenous vein (Eagle et al., 2004; Go et al., 2013). However, these autologous grafts often present geometry and mechanical-property mismatch and may sometimes be damaged or simply unavailable due to previous interventions (Harskamp et al., 2013; Morishita et al., 2002; Weintraub et al., 2012). Synthetic vascular substitutes such as Dacron® or ePTFE (GoreTex®), although suitable alternatives for the replacement of large diameter vessels (McClure et al., 2012), have failed to provide an appropriate substitute for small diameter blood vessels due to their low patency rates caused by mechanical and surface property mismatch that leads to thrombosis (Sarkar et al., 2009).

Alternative substitutes have therefore been developed by tissue engineering, combining cells and biomaterials to create living blood vessels. Different techniques are used to produce a tissue-engineered vascular construct. The first method uses a scaffold on which cells may be seeded. The scaffold is made of polymers that may be biodegradable (Leong et al., 2008; Stegemann et al., 2007; Kakisis et al., 2005) or alternatively decellularised animal or human tissues (Campbell et al., 2012; Schaner et al., 2004). A second method, called the self-assembly approach, entails using cells and their own extracellular matrix secreted in vitro to recreate the geometry of the substitute (L'Heureux et al., 1998, 2006). Both techniques provide control over the geometry of the substitute. They also offer the greatest potential to mimic the biological and mechanical properties of healthy native vascular tissues.

Regardless of the construction technique, a crucial characteristic of a vascular substitute is its ability to maintain its integrity under mechanical constraints induced by blood pressure. Therefore, the accurate assessment of the mechanical properties of the substitute, primarily its failure or burst pressure, is vital prior to the release of a graft for clinical use.

The ANSI 7198 standard (ANSI/AAMI/ISO 7198) that oversees the measurement methodology of the mechanical properties of tubular vascular prostheses lists two methods that may be used to evaluate the circumferential strength of a vascular substitute. These methods are presented as alternatives to one another and are both widely used in literature on vascular substitutes (Seliktar et al., 2003; Sheridan et al., 2012; Berglund et al., 2005; Weidenhamer and Tranquillo, 2013; Hoerstrup et al., 2001; Syedain et al., 2011; Soletti et al., 2010).

The first method, which will be referred to as the direct method, consists in pressurizing the construct with a fluid until failure, while directly measuring the applied pressure. The maximal recorded pressure corresponds to the burst pressure. This method has the advantage of applying the load in a physiological manner while allowing a direct measurement of the property of interest. It is considered in literature on vascular substitutes as the gold standard (Konig et al., 2009). However, it is a destructive method that requires a long vessel segment. These are usually not easily available since the production of tissue-engineered material requires special equipment and is costly and time consuming.

The second method is the ring tensile test. It requires a ring sample that is threaded on pins that are separated at a constant speed until the ring specimen fails. During the test, the pin displacement and the load resulting from pin displacement are measured. This load-application method is less similar to the physiological mechanism but since a significantly smaller specimen length is required, it offers a major advantage for testing tissue-engineered constructs. The ring tensile test method is therefore often used in literature. Since this test does not allow direct measurement of the burst pressure, Laplace's law is then applied to estimate the burst pressure from the results of a ring tensile test (Konig et al., 2009; Mauri et al., 2013; Nieponice et al., 2008; Berglund et al., 2004). This law is commonly used in physiology to describe the behavior of thin-walled cavities under pressure, such as blood vessels. It states that the wall tension of a pressurized cylinder is equal to the product of the pressure inside the cylinder and its radius (Burton, 1954; Valentinuzzi and Kohen, 2011).

Many research groups use both test methods in the same experiment. They evaluate the burst pressure of their substitutes by the direct method and use ring tensile tests to analyze the stress–strain relationship (Stankus et al., 2007; Sarkar et al., 2009). However, few groups assess the potential of Laplace's law to estimate the burst pressure of their construct from ring tensile test data by making a direct comparison with the direct measurement. When a comparison is made, a first study states that both methods lead to similar measured/estimated burst pressure (Stekelenburg et al., 2009). On the opposite, it has been pointed out by Konig and collaborators (Konig et al., 2009) that the estimated burst pressure obtained by a ring tensile test may be overestimated compared to a direct measurement. This conclusion was supported by the analysis of data reported by other research groups. However, rigorous comparison was proven difficult, primarily because tests conditions were not discussed. Indeed, as was previously reported (Sarkar et al., 2006), burst pressure measurement depends on tissue strain rate. There was however no way to ascertain that both direct measurement and ring tensile tests were performed in the same test conditions in both the referenced studies and the study itself.

Therefore, the main objective of this study is to present a straightforward and rigorous comparison of measurements performed by both methods in the same test conditions. The validity of Laplace's law to estimate the burst pressure of a vascular substitute from the results of a ring tensile test is first examined. The study is then pushed further by investigating the potential of ring tensile tests to estimate failure strain and stiffness of the vascular constructs.

Evaluation of mechanical properties is also highly dependent on the geometry of the sample tested. Transparent disclosure of measurement techniques is therefore crucial for adequate interpretation of the results. Thickness of the tissue, for example, is