Architecture Dependent Compressive Failure Modes in Scaffolds for Articular Cartilage Repair

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INTRODUCTION: Tissue engineering approaches involve seeding cells onto a porous scaffold with subsequent culturing to promote cell proliferation and matrix deposition[1,2]. Once implanted in patients, tissue engineered cartilage constructs may experience contact pressure greater than 10 MPa[3]. Such loading leaves implants vulnerable to structural failure, such as buckling, which compromises their in vivo mechanical function and large strains from the failure may also damage cells[4]. Understanding the compressive behavior of the collagen scaffold is crucial to preventing structural failures. Previous work has shown a relationship between increased matrix deposition and reduction of buckling[5], but the relationship between mechanics of collagen scaffolds and their architectures are poorly understood. The objective of this study is to identify the architecture dependent compressive behaviors of scaffolds for tissue engineering.

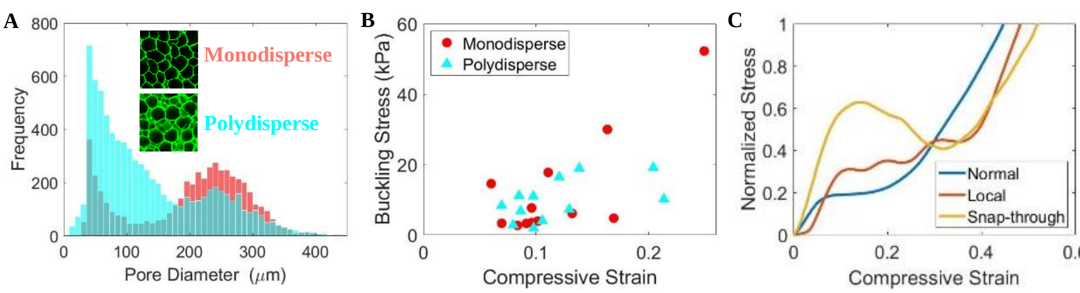
METHODS: Two different architectures of honeycomb collagen scaffold with the same aggregate mechanical properties were tested, one monodisperse (manufactured by Histogenics®) and one polydisperse (manufactured by Koken®). The architecture of collagen scaffolds was characterized by the pore size distributions using the 'Particle Analysis' tool on ImageJ. To characterize global stress strain behavior, 24 acellular collagen scaffolds, 3 mm diameter and 1.5 mm thick, were compressed under cyclic confined compression using a triangular waveform with an amplitude of 60% at a rate of 1 mm/s and force recorded at 20 Hz. Buckled points were quantified using stress and strain curves from confined compression testing. To obtain local visualizations of scaffold buckling, acellular collagen scaffolds, 6 mm diameter and 1.5 mm thick, were bisected longitudinally. The bisected constructs were fluorescently stained with DTAF and mounted to a custom Tissue Deformation Imaging Stage (TDIS) on an inverted confocal microscope. Each construct was subject to a cyclic triangular waveform displacement at 1 mm/s at an amplitude of 50% while force measurements were taken at a rate of 1000 Hz. Open source Digital Image Correlation (DIC) software[6] was used to track the deformation and quantify the resultant local strains.

RESULTS: Polydisperse and monodisperse scaffolds have peaks at the same pore diameters; however, the distribution profiles were different (Fig 1A). There was no difference in buckling stresses between the scaffold types (Fig 1B) indicating the global compressive behaviors are similar. The global scale stress-strain response from confined compression normally follows a pattern of a toe region, a linear region, a plateau region, and a densification region. However, some samples showed characteristic non-linear structural failure such as snap-through buckling (Fig 1C), where the stress decreased after the linear stress region. Such local and global non-linear phenomena were visually identified via confocal microscopy during unconfined compression, revealing that the local structural failure is governed by competition of local snap-through buckling, localization buckling fronts, and global buckling. During unconfined compression testing, polydisperse collagen scaffolds always failed at contact points, but the local collapse band was not visible (Fig 2A). However, structural failures with the monodisperse collagen scaffolds were clearly visible and identified (Fig 2B).

DISCUSSION: This study identified (i) the types of structural failures present within the collagen scaffold during axial compression, (ii) different failure mechanism depending on scaffold architecture, and (iii) established a relationship between local structural failures and global scale stress strain curves. Both types of scaffolds behaved similarly on the global scale. However, local failure mechanics were significantly different. We found polydisperse collagen scaffolds always fail at contact points and the collapse bands is not visible. In contrast, all failures are visible in monodisperse collagen scaffolds. This behavior is most likely due to the difference in stiffness between larger and smaller pores within the polydisperse collagen scaffold[7]. This difference in pore stiffness leads to the collapse of larger pores before smaller pores can collapse, preventing the formation of global collapse bands which could protect the tissue from being damaged prior to matrix deposition.

SIGNIFICANCE: Prevention of structural instabilities by optimizing scaffold design is critical for enhancing tissue engineered constructs' global function and compressive properties leading to a successful cartilage implantation.

REFERENCES: 1) Crawford+ 2009; 2) Crawford+ 2012; 3) Brown+ 1991; 4) Bartell+ 2015; 5) Middendorf+ 2017; 6) Blaber+ 2015; 7) Gaitanaros+ 2018



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Scaffold / Failure	Mono	Poly
Normal	6	6
Local	5	3
Snap-through	1	3

Figure 1: Global scale data. A) Pore size distribution of polydisperse and monodisperse collagen honeycomb; 23 samples for each type. Polydisperse collagen scaffolds have higher frequencies < 200 μm while monodisperse collagen scaffolds have higher frequency > 200 μm. B) Buckling points of monodisperse and polydisperse scaffolds. C) Normalized stress and strain curves of normal compression, local structural failure, and snap-through buckling during compression. D) Number of samples exhibiting different structural failures per scaffold type.

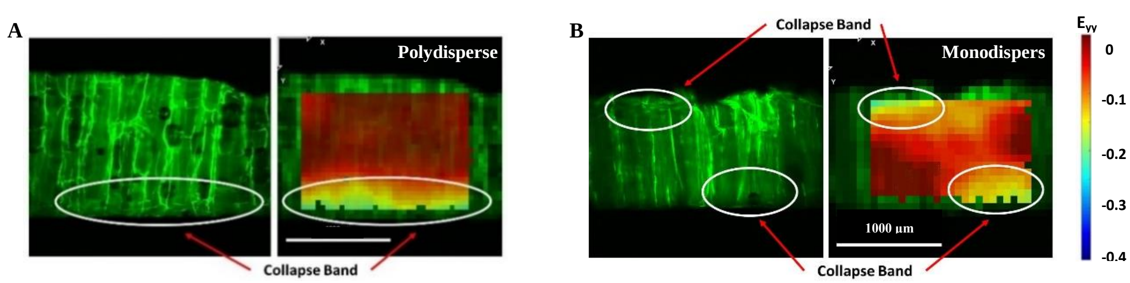

Figure 2: Local scale data. A) DIC data of a polydisperse collagen scaffold show the collagen scaffold failed at the bottom (contact point). B) DIC data of a monodisperse collagen scaffold shows multiple failed regions across depth.