Collagen scaffold porosity effects its mechanical, biodegradation and inflammation properties

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Statement of purpose: Collagen represents one of the most common and widely used biocompatible materials. While different collagen processing methods render implants with different stiffness, porosity, biodegradation and inflammatory responses, controlling these parameters independently still poses a challenge. For example, while a porous collagen scaffold allows for cell infiltration, it is often mechanically inadequate. On the other hand, improving collagen scaffold mechanical strength with crosslinking often leads to slow degradation and elevated inflammatory responses in *vivo* [1]. In this study we attempted to create mechanically robust collagen scaffolds and evaluate how scaffold porosity influences its mechanical properties, biodegradation rate and inflammatory responses.

Materials and Methods:

Sample preparation: Human tendons were first cleaned using the RTI proprietary BioCleanse® method [2, 3]. The tendons were acid hydrolysis to produce a collagen dispersion which was subsequently dried to different final collagen concentrations. This resulted in porous scaffolds with the following collagen concentrations: 87, 100, 194, 254, 338, 361 and 373 mg/cm^3. The scaffolds were sterilized with low dose Gamma irradiation and tested either mechanically or implanted in a rat animal model.

Mechanical test: Scaffolds were cut in a dog bone shape sample and tested in tensile pull-out configuration on Instron machine. From the pull-out tensile stress-strain curve, the ultimate tensile strength, failure load, failure strain and tensile modules, were calculated.

Rat implantations: Approximately 2-3 mg of scaffold material was implanted per intramuscular pouch in athymic rats. There were 5 study groups (100, 194, 254, 361 and 373 mg/cm^3) with six implants per group. The rats were sacrificed 6 weeks after implantation and examined for the presence or absence of implants. Histological cross-sections were evaluated for the remaining collagen and inflammatory response. The left-over collagen ("biodegradation") was graded on a scale from 0 to 2 where 0 was no sample and 2 was more than 50% sample remaining. The inflammation response was scored on the Edwards scale from 0 to 3 where 3 was highly inflammatory.

Results:

Histological appearance of collagen scaffolds ranged from densely packed lamellar to random void structures (Fig 1a,b). The ultimate tensile strength, failure load and stiffness significantly decreased with increasing porosity. Tensile stiffness (~ 87 MPa at 373mg/cm^3) decreased more than 6 fold with a 4 fold increase in porosity (Fig. 1c). The ultimate tensile strain ranged from 13% to 21% strain. Macroscopic evaluation at the time of sacrifice showed all 6 implants were present for the highest collagen scaffold density, while few or no samples remaining for the scaffolds with lower collagen densities. Similarly, the highest density scaffolds demonstrated minimal signs of degradation with minimal cell penetration (Fig. 2a). On the other hand, scaffolds with a density of 338 and 361 mg/cm^3 demonstrated less than 50% remaining in any cross-section. Independently of the group, inflammation was low with almost no fibrous capsule formation.

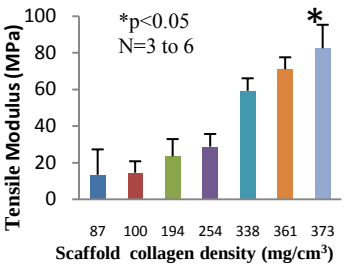

Figure 1c

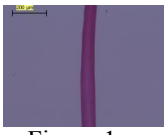

Figure 1a

Figure 1b

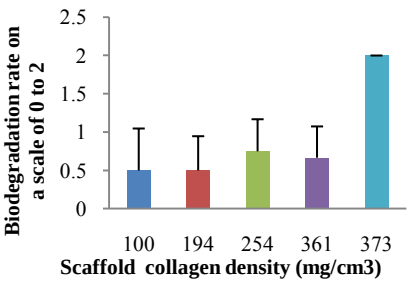

Figure 2c

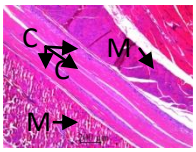

Figure 2a

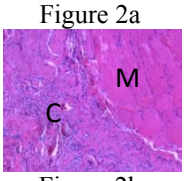

Figure 2b

Conclusions:

In this study we processed human tendons to create collagen scaffolds of different porosity. We showed that it is possible to create scaffolds with large initial stiffness without using additional chemical or physical crosslinking. Such collagenous scaffolds were also tailored for controlled implant degradation and low inflammation in rat model. In a clinical setting, these scaffolds may be used for guided tissue repair while providing easy handling and initially robust mechanical properties.

References: [1] Puchner AH at al.J Surg Res. 2008 Mar;145:105. 2007 [2] Schimizzi et al., AJSM. 2007; v35; 612. [3] Jones et al., Arthroscopy 2007: v23, p400.