PEG-based Hydrogels as Vocal Fold Regeneration Matrices

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Chronic voice impairment due to scarring of the vocal fold lamina propria (LP) can be debilitating in terms of quality of life. Current clinical management of this complex condition generally produces inconsistent and suboptimal results(1). Due to the size of the patient population suffering from voice impairment secondary to scarring, alternate treatment methods are needed. Researchers are therefore investigating a number of alternative treatments for LP scarring, including growth factors(2, 3), stem cells(4), biomaterial implants(5, 6). To date, most clinical and animal trials of biomaterial implants have focused on the efficacy of conventional augmentation substances(7), including collagen(8), fat(9), fascia(10), and hyaluronan (HA) (11), for the improvement of the biomechanical and biological properties of scarred LP.

Although collagen, HA, and fat have each resulted in some degree of improvement in VF function post-implantation, variability in the resorption and/or contraction of these materials, and hence variability in the degree of vibratory improvement, has limited the general success of these materials(1). In the present study, polyethylene-glycol (PEG)-based hydrogels are examined as potential vocal fold regeneration matrices. PEG has several properties desirable in a vocal fold regeneration template. Diacrylate-derivatized PEG (PEGDA) macromers readily dissolve in aqueous solution, forming an injectable mixture that is photopolymerizable through epithelial layers, a feature critical for a vocal fold regeneration scaffold, since vocal fold tissue is highly susceptible to scarring induced by surgical procedures(3). In addition, the photoactivity of PEGDA combined with its intrinsic resistance to cell and protein adhesion results in a biological “blank slate” (12) which can be modified in a controlled manner to contain bioactive moieties. PEG hydrogels are also highly elastic, which is important to the vocal folds which must sustain prolonged high frequency stresses, and their mechanical properties are tunable, meaning that their properties can be tailored to patient needs.

In this work, pig VFFs were encapsulated at ~0.5×10^6 cells/mL in the following precursor solutions, each containing 2 μmol/mL acryloyl-PEG-RGDS: (1) 10 (w/v) % 10000 Da PEGDA, (2) 20 (w/v) % 10000 Da, (3) 30 (w/v) % 10000 Da and cultured in the DMEM supplemented with 10% FBS, 100 mg/L, 100 mU/mL penicillin, and 100 mg/L streptomycin composites in a humidified incubator maintained at 5% CO_2 / 37 ºC. After 4 weeks and 8 weeks of culture, the constructs were examined biochemically, biomechanically, and histologically. All matrices tested successfully resisted fibroblast-mediated matrix compaction detrimental to vocal fold restoration. Moreover, we demonstrate that can tune VFF matrix production by altering the mechanical properties of the scaffold.

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