Dual Growth Factor Loaded Bioactive Injection Material for the Enhanced Treatment of Vocal Fold

1Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, 2Department of Advanced Materials, Hannam University
Hee-Jin Ahn1, Tae Ho Kim2, Mi Ri Park3, Mi-Jung Han1, Eun Jae Jung1, Tack-Kyun Kwon1, Jin Ho Lee, PhD2, Seong Keun Kwon, MD, PhD3

Background
The demand for the treatment of glottal insufficiency is increasing. Several injection materials have been examined for this purpose, however, biologic reabsorption, particle migration, and ongoing degradation of the injected materials, and thus the need to perform multiple injections still remain as major clinical problems. In this study, the two different (single basic fibroblast growth factor (bFGF), single hepatocyte growth factor (HGF), and dual bFGF/HGF) growth factor (GF) immobilized microbeads were investigated for their potential use as a bioactive injection laryngoplasty agent.

Methods
bFGF, HGH and dual GF were bound to heparin-immobilized PCL/F127 microbeads. Each growth factors were found to be continuously released over 35 days on a ELISA assay. Human Vocal Fold Fibroblast (hVFF) proliferated significantly more on bFGF and dual GF-immobilized microbeads, GF-immobilized microbeads (bFGF, HGF, and dual) were injected to the paralyzed vocal folds of New Zealand’s white rabbit, and four weeks later, rabbits were sacrificed and tissue around the injected vocal fold were dissected for RT-PCR and histology.

Results
There was no significant inflammatory sign on endoscope and H&E staining. Microbeads remained at the injection site, reading to the constant volume augmentation of paralyzed vocal fold without significant inflammation. The expression of extracellular matrix (ECM) gene related with the synthesis of collagen which are main substances of vocal fold was upregulated and collagen and HA deposition was enhanced by dual GF loaded microbeads which was confirmed by Masson’s Trichrome staining and Alcian Blue staining.

Conclusion
In conclusion, Dual GF loaded microbeads augmented the volume of the paralyzed vocal fold passively and induced the collagen and HA synthesis actively at the injected vocal fold. Dual GF loaded microbeads could be a new promising injection material for paralyzed vocal fold.

Keywords
Injection laryngoplasty, Growth factor, Collagen, Hyaluronic acid, Extracellular matrix, Lamina propria