A study of Injection therapy using b-FGF by High speed imaging and acoustic analysis

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Abstract
Human basic fibroblast growth factor (bFGF) promotes wound healing by accelerating formation of benign granulation tissue and epithelization. Several intracutaur injection materials are available today and each of them has advantages and disadvantages. Due to the characteristics, bFGF is expected to exert persistent effect with few complications. We started intracutaur injection of bFGF in cases with glottal insufficiency after informed consent to participation in the clinical study was obtained, and followed them up by high-speed digital imaging and acoustic analysis. After laryngopharyngeal anesthesia and laryngeal injection anesthesia, bFGF was injected into the vocal code with a peroral injection needle. For an injection material, Fibrast spray 250® (Kaken Pharmaceutical Co., Ltd., Japan) was diluted to 20 μg/ml and it was injected into the superficial part of the lamina propria mucosae or muscle layer. The first injection was, in principle, done unilaterally, and more than one injection was carried out in some cases. Glottic space and amplitudes were analyzed based on the images obtained by high-speed digital recording and fluctuation and noise components were analyzed based on phonetic data for evaluation of the efficacy of bFGF.

Introduction
Glottal insufficiency is induced by vocal code atrophy and paralysis. Our country is ranked first as an aging society in the world and the proportion of the elderly is expected to increase further in the future. Accordingly, patients with hoarseness due to atrophic vocal code disease are expected to increase. Intracutaur injection is one of the treatments for glottal insufficiency. For intracutaur injection, silicone, fat, fascia, and atherocollogel have been employed. Recently Hirano et al. used human basic fibroblast growth factor (bFGF) and showed its efficacy. We followed-up wave glottal waves in patients receiving intracutaur injection of bFGF with a high-speed video (HSV) recorder and examined the efficacy.

Methods and Materials
The subjects comprised 30 cases that received intracutaur bFGF injection at our hospital between 2012 and 2014. The breakdown of disease was: vocal code atrophy, 11 cases; sulcus, 12; and recurrent nerve paralysis, 7. There were 21 male and 9 female cases. The average age was 69.9 years and 23 patients were aged at 65 years or older. The follow-up period was 1 to 12 months and 7.2 months on average. More than one injection was carried out in 8 cases.

Results
There was a significant improvement after treatment both in “G” and “B” with regard to breathy hoarseness in the GRBAS scale (Figure 3 and 4). MPT was significantly longer after treatment (Figure 5). Of 30 cases, 15 cases that were examined by HSV images were subjected to image analysis. The minimum glottal distance and minimum glottal area were significantly improved after treatment. The effect persisted for 12 months (Figure 6 and 7). Meanwhile, the amplitudes of the vocal codes showed no change after treatment at the anterior, middle, and posterior part on either side (Figure 8 and 9). PPQ and APQ obtained from the sound recorded at the same time were significantly improved (Figure 10 - 12).

Discussion
In 1974, bFGF was found as a factor accelerating the migration of fibroblasts,7 and it has widely been employed for treatment of refractory ulcer and decubitus in Japan. As the underlying mechanism for wound healing, it accelerates angiogenesis and formation of granulation tissue and epithelium by promoting proliferation of keratinocytes and cells of mesenchymal origin, such as endothelial cells, fibroblasts, and vascular smooth muscle cells. In addition, it has been found that it plays an important role in not only rapid epithelialization of the wound but also prevention of scar contraction.1)

On the basis of these effects, intracutaur injection is expected to not only increase the mass of the vocal code but also help acquire excellent glottal waves. The minimum glottal area and minimum glottal distance measured by GWA decreased after the injection, which suggested the alleviation of glottal insufficiency. Aleviation of scar contraction was expected to increase glottal waves. However, there was no significant increase in the amplitudes of glottal waves in this analysis. Nevertheless, since acoustic analysis demonstrated an improvement in fluctuation of amplitudes and cycles, it was supposed that scar contraction was diminished to a certain degree.

Previous reports have demonstrated that accurate evaluation of glottal waves is possible by HSV recording. Furthermore, glottal wave analysis at arbitrary points and areas is possible with KIPS. HSV analysis was considered useful for a postoperative follow-up, determination of the timing of a re-operation, and selection of the injection site. More-than-one-year-long term outcomes of intracutaur injection of bFGF remains to be elucidated. We are planning to accumulate more cases and verify the efficacy.

Conclusions
We carried out intracutaur injection of bFGF and a follow-up by aerodynamic tests, acoustic analysis, and HSV recording. Aerodynamic tests and acoustic analysis revealed significant efficacy. HSV showed alleviation of glottal insufficiency. It was considered that a follow-up and analysis by HSV images was useful for not only evaluation of efficacy but also determination of future treatment strategies.

References