Absorption and migration study by CT

Patients and evaluation
An autopsy was performed, and with permission from the family, the larynx was resected for dissecting aortic aneurysm) died due to another cause about 4 months after injection laryngoplasty.

Methods:
Since 2003, injection laryngoplasty using CPC has been performed for 52 cases to manage glottic insufficiency due to unilateral laryngeal paralysis (average follow up period: 18.6 months, maximum: 41 months, minimum: 1 month). Volume and migration analysis for injected CPC using CT were performed at the time points of 1 month, 6 months, 1 year and 2 years after surgery on these patients. Vocal function was also assessed by measurement of G/R/BAS (phonatory function assessment) and VHI (voice handicap index) score. All these data were statistically compared using paired t-test.

Results:
The volume and position of injected CPC were stable on CT at all time periods observed.

Conclusions:
Our clinical experience revealed CPC was safe, nonabsorbable and effective. Injection laryngoplasty using CPC is useful in the treatment of glottic insufficiency.

Introduction
When performing injection laryngoplasty, the ideal injection material is one that causes little tissue reaction, remains at the injection site without being absorbed, and is easy to inject. Tissue compatibility is also important. Materials used to date, each with unique advantages and disadvantages, include Teflon, silicone, atelocollagen, and autologous tissues (fat and fascia). However, none of these materials fully meet these requirements. We have used calcium phosphate cement (CPC) to meet these requirements for injection laryngoplasty. CPC is an orthopedic filling paste that is used for bone replacement in patients with bone fractures and defects, has demonstrated clinical safety, and can easily be injected.

Calcium phosphate cement (CPC) (Biopex-R, Mitsubishi Phama) has been marketed since June 2000 as a medical material used mainly in orthopedic and neurosurgery. The kit contains forms of pastes and liquid that are mixed in the recommended ratio to become a paste (Fig. 1), which is then injected. CPC is a calcium phosphate salt that, when hardened, forms hydroxyapatite. Hydroxyapatite is the chief inorganic constituent of human bone and teeth, and because of high tissue compatibility, is widely used for artificial bone in surgical procedures. There is little foreign body reaction, almost no long-term absorption, and it is easy to prepare. This offers many advantages as a material for injection laryngoplasty.

We first tested CPC for injection laryngoplasty as rabbits and found no absorption and minimal foreign body reaction [1]. This suggested promise as a novel material for injection laryngoplasty in clinical settings. Based on our experimental findings, we received approval from the ethics committee to use CPC for injection laryngoplasty in clinical patients. Four years have passed since use in our first patient, and 52 patients have undergone this procedure to determine usefulness of CPC for injection laryngoplasty in clinical patients.

Patients and Methods
Surgical procedure
CPC (Biopex-R, 3 cc kit) (Fig. 1), Storz injector (model 27200), and 16- or 17-gauge injection needle 30 cm in length (Fig. 2) are used under microlaryngeal surgery setting. For transcricnosis injection, usually we use an 18-gauge short needle. The Biopex powder and liquid are then mixed in the recommended ratio to become a paste (Fig. 1), which is then injected. CPC is a hardening material, so it must be injected between the thyroarytenoid muscle and thyroid cartilage, or into the thyroarytenoid muscle on the paralyzed side, with care to avoid submucosal injection.

Results:
3 days after injection
2 years after injection

Phonatory function
Phonatory function was assessed in 38 of 52 patients by CPC (maximum phonation time), G/R/BAS, and acoustic analyses. Fig. 4 shows the changes in CPC over time in the 18 patients. The mean CPC before surgery was 4 seconds, by 1 month postoperatively, there was a significant improvement in CPC to 9 to 30%.

Discussion
Hydroxyapatite granules with gel have recently been used in the United States for injection laryngoplasty with good clinical results [3,3]. However, in studies using this material, absorption after injection of the gel used as a carrier for the hydroxyapatite granules has been reported. Thus, only the hydroxyapatite granules remain, thus causing marked changes in volume after injection. This differs from CPC, which we used in our series of patients. CPC hardens after injection to form hydroxyapatite by a hydration reaction. The injected material forms a mass with almost no change in volume. In addition, unlike granules, there is little dispersion, thus making CPC more preferable as a material for injection laryngoplasty. In a preclinical study, we also tested CPC for injection laryngoplasty in rabbits [1]. At 1, 3, and 4 months after injection, histologic examination showed only minimal foreign body reaction, no evidence of migration, and very little absorption, with almost 90% of the injected volume present after injection.

Fifty-two patients have undergone the procedure to date. The procedure can be performed safely, and no acute side reactions immediately after injection have occurred. Patients have been followed up for 1 year, and no absorption, migration, or excretion of the injected material has been observed. In addition, evaluation of postoperative voice function has shown significant improvement. Our findings demonstrate that CPC is safe and effective as an injection material.

Pharmacologic properties of CPC may be unique and this makes CPC suitable for application in injection laryngoplasty. As observed in the resected larynx in Fig. 7, our procedure involves injection of the hardening material (injectable blocks) into the lateral part of the vocal cord to achieve vocal cord medilization, which may be considered as “endothoracic type” in CPC may show different pharmacologic properties.

Fig. 3
Fig. 4
Fig. 5
Fig. 6
Fig. 7
Fig. 8

References

Fig. 1
Calcium Phosphate Cement (CPC), Biopex-R
powder
liquid
Injectable
paste
Hydroxyapatite
Block
Fig. 2
CPC

Fig. 3
Phonatory function
Examination of the larynx resected at autopsy 4 months after injection laryngoplasty showed a hardened mass where the CPC had been injected between the thyroarytenoid muscles and thyroid cartilage, without any absorption or migration (Fig. 7). Histological examination revealed only a mild foreign body reaction (Fig. 8A).