1. Summary of your presentation (Include what you learned from discussions with audience)

The wound healing mechanism of vocal fold is composed of 3 overlapping phases: inflammatory, proliferative, and remodeling. Several important elements including cells, cytokines, growth factors and extracellular matrix (ECM) have been confirmed to contribute in successful wound healing. However it is not still unclear whether or not a wound is to be repaired completely or scarred. Fibroblasts have received widespread attention as the main provider of ECM during proliferative and remodeling phases. In other areas, however, more immature cells including stem cells or born marrow derived cells have proven to play an important role in tissue regeneration after wound. Side population (SP) cells are known as the stem cell enriched population, and have stem cell like characteristics. Earlier, we demonstrated the existence of SP cells in the human vocal fold, and this study was designed to determine how these cells work during wound healing of rat vocal folds.

The vocal folds of Sprague Dawley rats, aged 13 weeks, were unilaterally scarred by incision of the lamina propria. The larynges were harvested at each week until five weeks after procedure, and coronal cryosections were made. Immunohistochemistry was performed with anti-ATP binding cassette subfamily G member 2 (ABCG2) antibodies to detect SP cells in the rat vocal fold. SP cells have the ability to exclude the DNA binding dye, Hoechst 33342, and this ability makes them positive to ABCG2. Each positive cell was analyzed at three portions; anterior macula flava, Reinke's space and posterior macula flava, and the injury side of vocal folds compared with the contra lateral normal side at each time point. Immunohistochemistry showed that there were ABCG2 positive cells in anterior macula.
flava and the posterior macula flava, but there was no significant difference between normal and injured sides. ABCG positive cells appeared in the Reinke’s space at 1 week on the injured side, while rare expression was found on the normal side. The expression of SP cells on the injured side disappeared after 2 weeks. The current study indicated expression of SP cells in the injured Reinke’s space of rat vocal folds in relatively early stage of wound healing. The contribution of SP cells was in vocal fold wound healing has been proven, although further study is in need to clarify their roles for tissue repair.
2. Other topics of your interest

"Reactive response of fibrocytes to vocal fold mucosal injury in a rat"

The vocal fold mucosa plays an important role in voice production. Its cellular composition and density frequently change under various pathological conditions, often contributing to altered extracellular matrix production, tissue viscoelasticity, and voice quality. In this study, cellular changes in the rat mucosa following a unilateral stripping injury were investigated and analyzed semi-quantitatively. Distinctive and sequential changes in cellular morphology, composition, and density were observed in the mucosa post-injury. Cellular recruitment was a major event during the early stage of injury and reached its peak level by day 5 post-injury. Several types of cells, including neutrophil-like cells, epithelial cells, and fibrocytes, were sequentially recruited. The sequential emergence of reactive cell populations following injury and subsequent reconstruction of the mucosa suggests their involvement in vocal fold tissue repair and scar formation processes.

"Restoration of chronic vocal fold scar with hepatocyte growth factor hydrogel"

Therapeutic challenges exist in the management of vocal fold scarring. We have previously demonstrated the therapeutic potential of hepatocyte growth factor (HGF) in the management of acute phase vocal fold scarring using a novel hydrogel-based HGF drug delivery system (DDS). However, the effect of HGF on matured vocal fold scarring remains unclear. The current study aims to investigate the effect of HGF-DDS on chronic vocal fold scarring using a canine model. Vocal folds from eight beagles were unilaterally scarred by stripping the entire layer of the lamina propria; contralateral vocal folds were kept intact as normal controls. Six months after the procedures, hydrogels (0.5 mL) containing 1 microg of HGF were injected into the scarred vocal folds of four dogs (HGF-treated group). Hydrogels containing saline solution were injected into the other four dogs (sham group). Histological and vibratory examinations on excised larynges were completed for each group 9 months after the initial surgery. Experiments conducted on excised larynges demonstrated significantly better vibrations in the HGF-treated group in terms of mucosal wave amplitude. Although phonation threshold pressure was significantly lower in the HGF-treated group compared with the sham group, no significant differences were observed in the normalized glottal gap between HGF-treated and sham groups. Histological examinations of the HGF-treated vocal folds showed reduced collagen deposition and less tissue contraction with favorable restoration of hyaluronic acid. Results suggest that administration of HGF may have therapeutic potential in the treatment of chronic vocal fold scarring.
Hands-on workshops are a centerpiece of the Phonosurgery Symposium. Each participant can select several workshops with various surgical and behavioral assessment and treatment techniques, and works with special voice disorder populations. I selected “Voice boot camp”, “Arytenoid adduction and abduction”, “Microflaps & Phonomicrosurgery” and “Stroboscopy”. All of them are impressive, and unforgettable.
3. Impression of the meeting you got (e.g., major trends in the field, status and contribution of your study and/or studies in Japan to the field, etc.)

These conferences and the symposium are designed to increase basic scientific knowledge, improve clinical practice, help practitioners make decisions about appropriate treatment, and showcase new techniques by leading scientists, speech pathologists and surgeons. In this meeting, I impressed that many actors are trying to treat voice disorders. Otolaryngologists, speech pathologists, basic and voice scientists, and other clinicians influence one another.

It is still unknown how the regenerative process works in the vocal fold, or even whether stem cells, responsible for tissue regeneration, exist in the vocal fold. I have been searching for tissue specific stem cell of vocal folds. In this field, Leydon C et al. reported “Distribution of putative stem cells in vocal fold epithelium”.

Although we can deal with many types of vocal fold pathology, vocal fold scarring remains a clinical challenge. Regenerative therapy using stem cells including born marrow derived cells or adipose derived cells for the treatment of vocal fold scarring is a very active area of research in Otolaryngology. If we recognize the vocal fold specific stem cells, these cells will be useful sources of vocal folds regeneration.