Rhinology, 46, 317-323, 2008

# Histological study of expanded polytetrafluoroethylene (Gore-Tex®) implanted in the human nose*

Chan Hum Park

Department of Otorhinolaryngology-Head and Neck Surgery, College of Medicine, Hallym University, Chunchon, Korea

SUMMARY

*In rhinoplasty, various materials are used for nasal augmentation. Among these, expanded polytetrafluoroethylene (Gore-Tex®) is commonly used because of its supposed high biocompatibility. However, most studies regarding histological changes associated with its implantation have been carried out in animal models, and very few data are available from long-term human studies. We used light and electron microscopy to investigate the histological changes associated with expanded polytetrafluoroethylene in nasal augmentation in 30 patients. Histologically, connective tissue ingrowth was observed in all specimens. However, the degree of foreign body reaction and collagen deposition varied from specimen to specimen and had no apparent relationship with duration. Neovascularization was observed in specimens with durations longer than 12 months, and degenerative calcification was observed in a 36-month-duration specimen. Unlike the findings in previous reports, differences among individual responses, degenerative changes, and partially calcified lesions were observed in the expanded polytetrafluoroethylene. Based on this study, expanded polytetrafluoroethylene is a biocompatible material, but further long-term studies are necessary to address histological changes associated with the implantation of the material in the human nose.*

*Key words: biocompatibility, connective tissue, neovascularization, rhinoplasty*

## INTRODUCTION

In most Asian nations, nasal augmentation is the most popular nasal plastic surgery procedure. Although various materials have been used in nasal augmentation, we have yet to find an ideal, biocompatible material for use in nasal augmentation. Recently, expanded polytetrafluoroethylene (Gore-Tex®) has been reported to be suitable for use in the body, with low tissue reactions and long-term stability (1), and it has been used in many rhinoplasties [(2-8)]. Although there are some reports on histological changes associated with the implantation of expanded polytetrafluoroethylene in surrounding tissues in animal models, to our knowledge there are no detailed reports on the histological changes associated with its use in human nasal augmentation. Thus, we sought to investigate the histological changes in the surrounding tissues of the human nose associated with implantation of expanded polytetrafluoroethylene and to determine the changes in the expanded polytetrafluoroethylene when implanted in the human nose.

## MATERIALS AND METHODS

### *Subjects*

The subjects for this research were 30 patients who underwent nasal augmentation (sheet shaped Gore-Tex® is 2mm thick and usually, according to the intended degree of augmentation, a sheet 8mm wide should be multilayered with two fold (4mm)~three fold (6mm)) during the period from March 2000 to June 2005 and who were subsequently operated on again, for solely cosmetic reasons, without any infection or inflammation. The subjects consisted of 26 women and four men. The youngest subject was 22 years old, and the oldest was 46; the average age was 29. In all cases, revision second surgery was performed exclusively for cosmetic reasons. There were no any changes of the overlying skin. The expanded polytetrafluoroethylene that had been inserted in the first operation and the tissues that surrounded it were collected before conducting a further nasal augmentation procedure using various implants (sheet shaped Gore-Tex or reinforced Gore-Tex, W.L Gore & Associates Inc, Flagstaff, AZ. The price of the implant is approximately 300 euros in Korea). The second surgery was conducted 2 to 36 months after the first operation. The numbers of subjects having a second surgery after 2 months was three; after 3 months, five; after 6 months, eight; after 8 months, four; after 12 months, four; after 15 months, four; and after 36 months, two (Table 1).

*Received for publication: January 28, 2008; accepted: July 3, 2008

*Macroscopic observation*

During the second surgery, we observed the shape of the expanded polytetrafluoroethylene, the level of adhesion to surrounding tissues, and whether there was evidence of inflammation around the expanded polytetrafluoroethylene.

*Observation using an optical microscope*

Part of the expanded polytetrafluoroethylene and surrounding tissues collected during the second surgery was fixed in 10% neutral formalin and processed for embedding in paraffin. Sections were cut at 5 μm and stained with hematoxylin and eosin (H&E). We observed the level of ingrowth of connective tissue into the expanded polytetrafluoroethylene, inflammatory and foreign body reactions, neovascular proliferation and calcification. In addition, the form and properties of the collagen between the expanded polytetrafluoroethylene and the surrounding tissues was observed, using Masson's trichrome stain. The extent of ingrowth of connective tissues and the properties and form of collagen between the expanded polytetrafluoroethylene and surrounding tissues were scored as moderate (+) if found only in the upper portion of the expanded polytetrafluoroethylene, severe (++) if found in the center portion as well, and negative (–) if not observed at all. For inflammatory and foreign body reactions, weak reactions were classified as moderate (+); strong reactions, as severe (++); and no reaction, as negative (–). Slight neovascular proliferation was classified as moderate (+); much proliferation, as severe (++); and no proliferation, as negative (–).

Table 1. Data of patients.

| | Sex | Age (years) | Operative method in 1st rhinoplasty | Causes for 2nd rhinoplasty | Intervals (months) |
|---|---|---|---|---|---|
| 1 | M | 22 | Aug, CR, Tip | Slightly deviated dorsum | 2 |
| 2 | F | 23 | Aug, CR, Tip | Irregular nasal dorsum | 2 |
| 3 | M | 27 | Aug, CR, Tip | Irregular nasal dorsum | 2 |
| 4 | F | 26 | Aug, CR, Tip | Slightly deviated dorsum | 3 |
| 5 | F | 31 | Aug, CR, Tip | Irregular nasal dorsum | 3 |
| 6 | F | 34 | Aug, RR, Tip | Remained hump | 3 |
| 7 | F | 25 | Aug, Tip | Asymmetric nostril | 3 |
| 8 | F | 23 | Aug, Tip | Asymmetric nostril | 3 |
| 9 | F | 24 | Aug, Tip | Asymmetric nostril | 6 |
| 10 | F | 23 | Aug, Tip | Overcorrection of nasal dorsum | 6 |
| 11 | F | 27 | Aug, CR, Tip | Slightly deviated dorsum | 6 |
| 12 | M | 32 | Aug, CR, RR, Tip | Slightly deviated dorsum | 6 |
| 13 | M | 25 | Aug, CR, Tip | Slightly deviated dorsum | 6 |
| 14 | F | 35 | Aug, RR, Tip | Undercorrection of nasal dorsum | 6 |
| 15 | F | 32 | Aug, Tip | Overcorrection of nasal dorsum | 6 |
| 16 | F | 25 | Aug, Tip | Overcorrection of nasal dorsum | 6 |
| 17 | F | 46 | Aug, Tip | Undercorrection of nasal dorsum | 8 |
| 18 | F | 29 | Aug, CR, Tip | Slightly deviated dorsum | 8 |
| 19 | F | 29 | Aug, Tip | Undercorrection of nasal dorsum | 8 |
| 20 | F | 29 | Aug, Tip | Undercorrection of nasal dorsum | 8 |
| 21 | F | 26 | Aug, Tip | Slightly deviated dorsum | 12 |
| 22 | F | 29 | Aug, Tip | Slightly deviated dorsum | 12 |
| 23 | F | 27 | Aug, Tip | Slightly deviated dorsum | 12 |
| 24 | F | 30 | Aug, Tip | Undercorrection of nasal dorsum | 12 |
| 25 | F | 40 | Aug, CR, Tip | Undercorrection of nasal dorsum | 15 |
| 26 | F | 29 | Aug, Tip | Undercorrection of nasal dorsum | 15 |
| 27 | F | 25 | Aug, CR, Tip | Slightly deviated dorsum | 15 |
| 28 | F | 24 | Aug, RR, Tip | Undercorrection of nasal dorsum | 15 |
| 29 | F | 35 | Aug, Tip | Slightly deviated dorsum | 36 |
| 30 | F | 35 | Aug, Tip | Slightly deviated dorsum | 36 |

**Aug: augmentation** **CR: corrective rhinoplasty,**
**Tip: tip surgery** **RR: reduction rhinoplasty**

*Observation using a scanning electron microscope (SEM)*

A 5 × 5-mm piece of the expanded polytetrafluoroethylene and surrounding tissues was excised, fixed in 1% glutaraldehyde (pH 7.4) containing 1% paraformaldehyde, and then rinsed in 0.12 M cacodylate buffer (pH 7.4). The tissue slices were secondarily fixed in 2% osmium tetroxide fixative for 90 min, dehydrated using alcohol and acetone, and dried using a critical-point dryer (Hitachi HCP-2). The dried samples were coated using an Eiko IB III ion coater and observed under a scanning electron microscope (Hitachi S-2500).

Table 2. Optical microscopy observations.

| Interval (months) | Connective tissue in-growth | Foreign body reaction | Neovascular proliferation | Collagen deposition | Calcification |
|---|---|---|---|---|---|
| **2** | + | + | – | + | – |
| **2** | + | – | – | + | – |
| **2** | + | – | – | + | – |
| **3** | + | – | – | + | – |
| **3** | ++ | + | – | + | – |
| **3** | ++ | – | – | + | – |
| **3** | ++ | + | – | + | – |
| **3** | ++ | + | – | + | – |
| **6** | + | – | – | + | – |
| **6** | ++ | – | – | + | – |
| **6** | ++ | – | – | + | – |
| **6** | + | + | – | + | – |
| **6** | ++ | – | – | ++ | – |
| **6** | ++ | + | – | + | – |
| **6** | ++ | + | – | + | – |
| **6** | ++ | ++ | – | + | – |
| **8** | ++ | ++ | – | ++ | – |
| **8** | + | – | – | + | – |
| **8** | + | – | – | + | – |
| **8** | ++ | + | – | + | – |
| **12** | ++ | + | + | + | – |
| **12** | ++ | + | + | + | – |
| **12** | ++ | + | + | + | – |
| **12** | ++ | + | + | ++ | – |
| **15** | ++ | + | – | ++ | – |
| **15** | ++ | ++ | + | + | – |
| **15** | ++ | + | ++ | ++ | + |
| **15** | ++ | + | ++ | ++ | – |
| **36** | ++ | ++ | ++ | + | – |
| **36** | ++ | – | + | + | ++ |

– : negative, + : moderate, ++ : severe

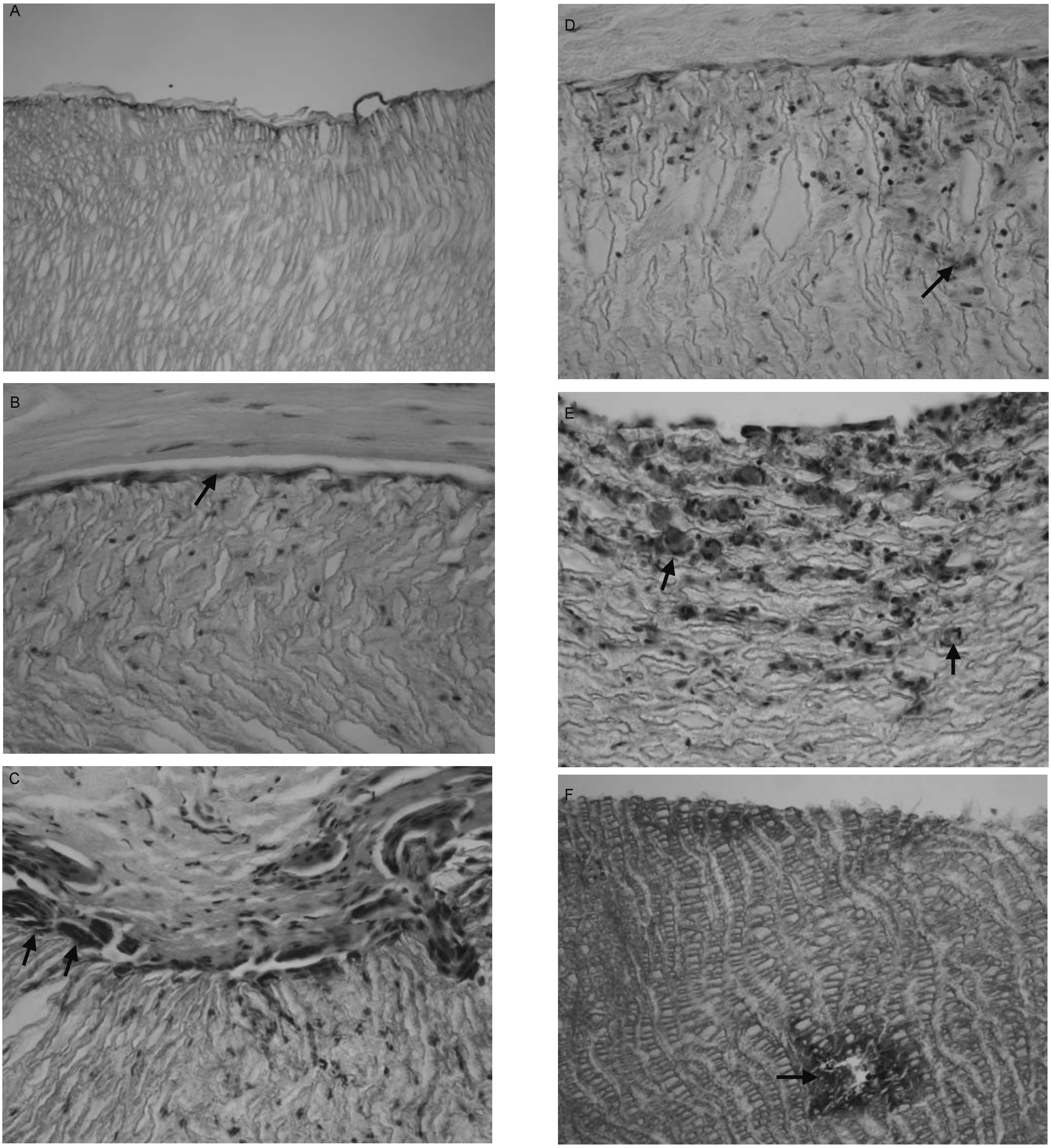



Figure 1. Histological sections of expanded polytetrafluoroethylene (Gore-Tex) by light microscopy (H&E stain). (A) At 3 months after primary rhinoplasty. Photomicrograph shows connective tissue incorporation and in-growth (×100); (B). At 6 months after primary rhinoplasty. Photomicrograph shows more connective tissue incorporation and in-growth than at 3 months. Note surrounding connective tissue with no foreign body reaction, and the thin fibrous tissue capsule (arrow) (×200); (C) At 6 months after primary rhinoplasty. Note surrounding connective tissue with severe foreign body and inflammatory reactions (arrows) (×200); (D) At 12 months after primary rhinoplasty. Note erythrocytes and neovascular structures within the expanded polytetrafluoroethylene (arrow) (×200); (E) At 15 months after primary rhinoplasty. Note the more prominent neovascular structures within the expanded polytetrafluoroethylene (arrows) (×200); (F) At 36 months after primary rhinoplasty. Note the calcified lesion of degenerative changes within the expanded polytetrafluoroethylene (arrow) (×100).

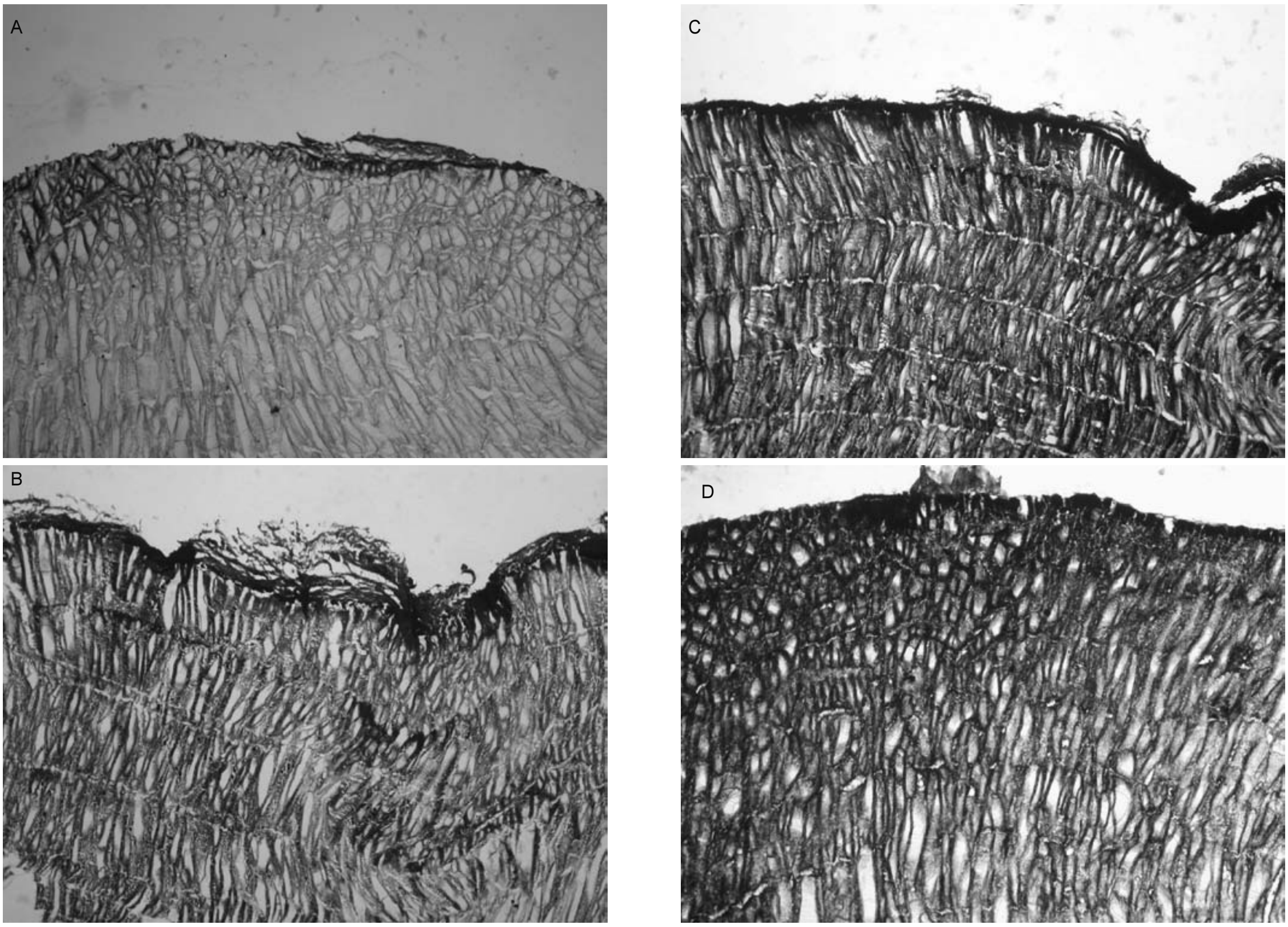



Figure 2. Histological section of expanded polytetrafluoroethylene by light microscopy (Masson's trichrome stain). (A) At 3 months after primary rhinoplasty. Note the weakly stained collagen fibers within the expanded polytetrafluoroethylene (×100); (B). At 6 months after primary rhinoplasty. Photomicrograph shows stronger staining than at 3 months. The expanded polytetrafluoroethylene was stained up to the central portion (×100); (C) At 15 months after primary rhinoplasty. Photomicrograph shows stronger staining within the expanded polytetrafluoroethylene than at 6 months (×100); (D). At 36 months after primary rhinoplasty. Photomicrograph shows stronger staining within the expanded polytetrafluoroethylene than at 15 months (×100).

## RESULTS

### *Macroscopic examination*

Although the collected expanded polytetrafluoroethylene showed a tendency to adhere more tightly to the surrounding tissue with increased time inside the body, we did not observe the formation of a strong tissue capsule, which can occur with silicone implants. Additionally, the separation of the expanded polytetrafluoroethylene from the surrounding tissues was not difficult, and no evidence of inflammation or infection was observed by macroscopic observation. Although parts of the collected expanded polytetrafluoroethylene showed evidence of having been folded, in most cases the expanded polytetrafluoroethylene maintained its original form and was slightly thinner.

### *Examination by optical microscopy*

All of the collected expanded polytetrafluoroethylene showed connective tissue infiltration, with greater connective tissue ingrowth at longer times inside the body (Figures 1 and 2). Connective tissue ingrowth was greater in materials that had been inside the body for 6 months compared with those that had been inside the body for 3 months, and connective tissue ingrowth increased until 12 months (Figures 1 and 2). Some cases showed increased connective tissue incorporation and ingrowth with no inflammatory or foreign body reaction (Figure 1B), whereas other cases showed increased connective tissue incorporation and ingrowth and exhibited severe inflammatory and foreign body reactions (e.g., Figure 1C). These cases were not related to the time of implantation (Table 1). Neovascular proliferation within the expanded polytetrafluoroethylene was first observed in cases in which the material had been inside the body for 12 months. Although the neovascular structures were not in the form of complete vessels, we observed erythrocytes and cells penetrating into the expanded polytetrafluoroethylene along irregular vessels (Figure 1D). At 15 months after implantation, we observed more prominent proliferation of neovascular structures, with vessel walls and with erythrocytes inside newly formed vessels (Figure 1E). Calcification, a manifestation of tissue degeneration, was observed in material that had been inside the body for 36 months. In this tissue, a partially calcified lesion within the expanded polytetrafluoroethylene and evidence of degenerative changes in the expanded polytetrafluoroethylene material itself were observed (Figure 1F). Lesions of collagen within the expanded polytetrafluoroethylene were observed in all tissues, and the stainability of the expanded polytetrafluoroethylene generally increased with increased time in the body (Figure 2). However, the severity varied among individuals, regardless of time (Table 2).

*Examination by scanning electron microscopy*

Similar to optical microscopy, the scanning electron microscope revealed ingrowth of surrounding connective tissue. Collagen increased with increased time in the body. The ingrowth of surrounding connective tissues at 2 months after primary rhinoplasty had appeared weak when observed by optical microscopy but was more prominent under the scanning electron microscope. The ingrowth of surrounding connective tissue showed a tendency to increase as time in the body increased (Figures 3 A-F). At 3 months, the ingrowth of connective tissue within the internodal space of the expanded polytetrafluoroethylene had increased, and the size of the internodal space had decreased (Figure 3B). At the surface of the expanded polytetrafluoroethylene, the connective tissue layer surrounding the internodal space was thicker at 6 months than at 3 months (Figure 3C). We observed erythrocytes and inflammatory cells in the internodal space in some, but not all, materials that had been implanted for more than 6 months (Figure 3C). With increasing time in the body, the ingrowth of connective tissues within the internodal space of the expanded polytetrafluoroethylene increased and filled the space. Thus, we observed the size of the internodal space decreasing. Especially in materials that had been implanted 36 months earlier, the connective tissue surrounding the expanded polytetrafluoroethylene was so thick that it was hard to differentiate between the expanded polytetrafluoroethylene and the connective tissues (Figure 3F).

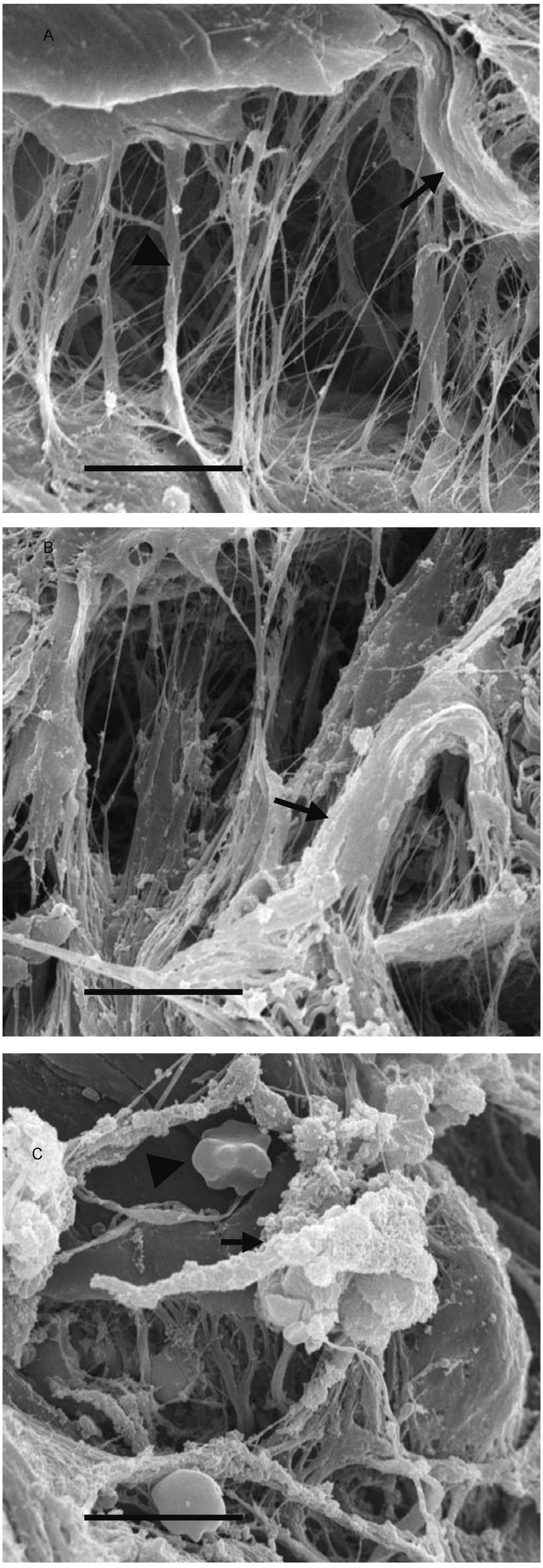
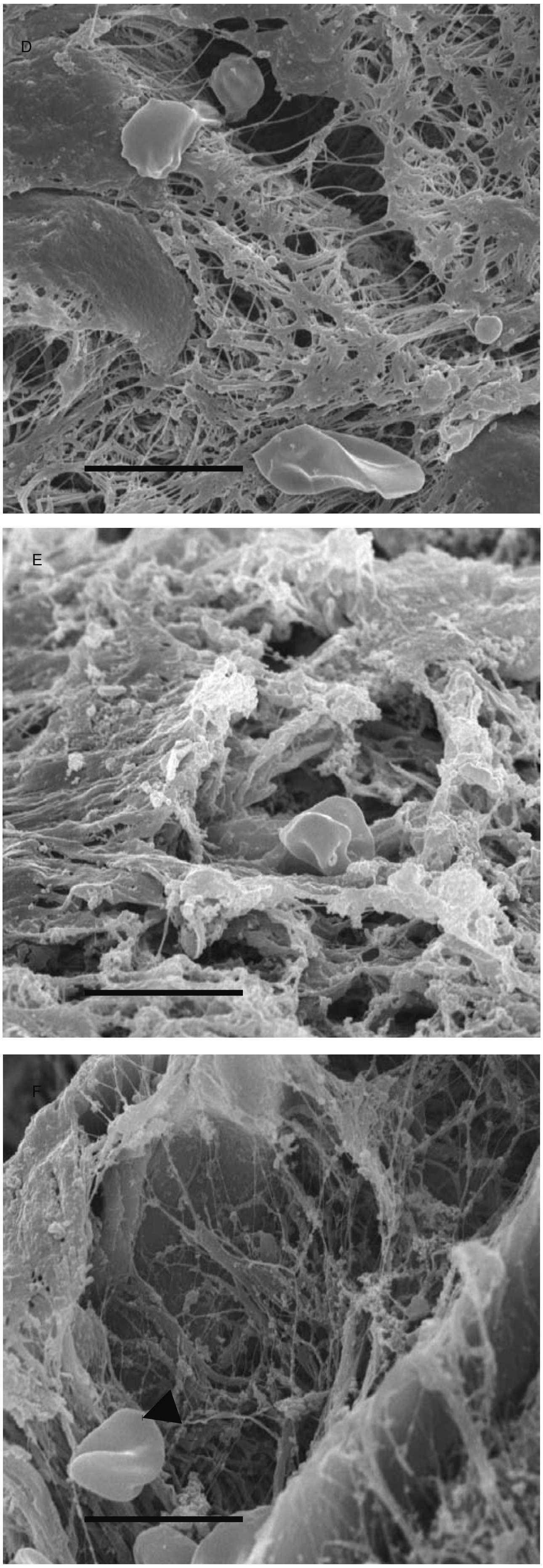



Figure 3. Scanning photomicrographs of expanded polytetrafluoroethylene (bar: 10  m): (A) At 2 months after primary rhinoplasty. Note the fibrils of polytetrafluoroethylene (arrow head) and connective tissue in-growth (arrow) (×3000); (B) At 3 months after primary rhinoplasty. Note thicker connective tissue in-growth (arrow) than at 2 months (×3000); (C) At 6 months after primary rhinoplasty. Note erythrocyte (arrow head) and inflammatory cells (arrow) within internodal space (×3000); (D) At 12 months after primary rhinoplasty. Note the surface of expanded polytetrafluoroethylene coated with more connective tissue (×3000); (E) At 15 months after primary rhinoplasty. Note fibrocytes and connective tissue filling the internodal spaces (×3000); (F) At 36 months after primary rhinoplasty. Note thick surrounding connective tissue and erythrocytes (arrow head) (×3000).




DISCUSSION

Among the materials that can be used in nasal augmentation, a patient's own cartilage is the ideal implant [9]. However, the use of a patient's cartilage presents several difficulties: additional surgery of the nasal septum and/or pinna is required to acquire the cartilage; the amount of cartilage that can be collected is limited; the collected cartilage cannot be used in re-surgery; implanted cartilage is susceptible to absorption; the external surface of the nose can become irregular; and the cartilage can easily be damaged by even the most minor trauma [10]. To overcome these shortcomings, xenograft implants with similar biocompatibility are required; expanded polytetrafluoroethylene (Gore-Tex®), a porous implant, has recently been widely used. Expanded polytetrafluoroethylene was invented in the late 1960s, and its safety has been demonstrated by its use in vascular surgery for 20 years. In 1993, it was approved by the US FDA for use in aesthetic surgery, including rhinoplasty [11].

Structurally, expanded polytetrafluoroethylene, a polymer with a molecular weight of 400-10,000 kDa, is formed by the polymerization of monomers that are connected by two double-bonded carbon atoms and four fluorine atoms. The negatively polarized fluorine atoms stabilize the carbon atom chain. As a result, polytetrafluoroethylene elicits a very limited inflammatory response and shows good anallergic biocompatibility. Connective tissues such as fibroblasts, capillaries, and collagen grow into the pores of implanted expanded polytetrafluoroethylene [12].

In New Zealand White rabbits, Mass et al. found some inflammatory cells and an inflammatory response in tissues implanted 3 weeks earlier with expanded polytetrafluoroethylene, but no ingrowth of connective tissue was observed. After the material had been implanted for 6 months, the ingrowth of connective tissue was observed, along with a decreased inflammatory response and reduced number of inflammatory cells. The material that had been implanted for 12 months appeared similar to that at 6 months, except a fibrous capsule was observed [13].

In the present study, the ingrowth of connective tissue was observed at 2 months after implantation in human patients, by both light and electron microscopy. With increasing time, the ingrowth of connective tissue increased, eventually filling the pores of the expanded polytetrafluoroethylene.

We observed some cases with no inflammatory cells or response and others with intense foreign body reactions, inflammatory cells, and an inflammatory response. These findings seemingly had no relationship with the elapsed time of the expanded polytetrafluoroethylene implant in the patient. It is possible that the extent of contamination varied in the implantation of the expanded polytetrafluoroethylene, but it seems more likely that the patients had different responses to the material. Further, the levels of collagen deposition also varied, again apparently without connection to the length of time the implant had been in the patient.

The outgrowth of new capillaries within the expanded polytetrafluoroethylene was observed. Partial capillaries were apparent in material at 12 months after implantation, and complete capillaries with strong vessel walls were seen at 15 months after implantation.

In materials that had been implanted more than 12 months earlier, cells had moved to the central portion of the expanded polytetrafluoroethylene and the ingrowth of connective tissue had taken place. It has been reported that the ingrowth of connective tissue into the expanded polytetrafluoroethylene maintains the fixation and stability of the implant after surgery and minimizes contracture by decreasing the capsule surrounding it [(12)]. Similarly, in this study, we saw no capsular construction when the expanded polytetrafluoroethylene was removed.
Expanded polytetrafluoroethylene is flexible and soft compared with other materials, but it is also relatively weak [(12)]. In this study, the implanted expanded polytetrafluoroethylene became thinner over time, probably because the pores within the material were squeezed by the pressure of the surrounding tissue after implantation. By electron microscopy, it was seen that the pores were prevented from getting much smaller as connective tissue ingrowth filled the space; thus, the expanded polytetrafluoroethylene could maintain a certain volume even under such pressure.

Previous studies found no histological deformity or absorption of the implanted expanded polytetrafluoroethylene [(3,13)]. However, in our study, calcification, a manifestation of degeneration, was observed in the expanded polytetrafluoroethylene 36 months after implantation.

## CONCLUSION

In this study, we observed that connective tissue ingrowth, inflammatory and foreign body reactions, and neovascularization increased with increasing time after implantation. However, there were considerable differences in reactions among individuals. Histological changes were observed over the long term in the expanded polytetrafluoroethylene implanted in the human nose. Additional long-term studies are necessary to further explore these histological changes of implanted expanded polytetrafluoroethylene.

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Chan Hum Park
Department of Otorhinolaryngology-HNS
Chunchon Hospital School of Medicine
Hallym University
153 Kyo-Dong
Chunchon, Kangwon
Korea 200-704

Tel: +82-33-252-9970
Fax: +82-33-241-2909
E-mail: hlpch@paran.com