Membranes for the Guided Bone Regeneration

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Abstract

Many kinds of membrane have been used for the guided bone regeneration (GBR) technique. However, most membranes do not fulfill all requirements for the ideal membrane for the GBR technique. Among them, collagen membrane has been most widely used. However, its high price and weak tensile strength in wet condition are limitations for wide clinical application. Synthetic polymers have also been used for the GBR technique. Recently, silk based membrane has been considered as a membrane for the GBR technique. Despite many promising preclinical data for use of a silk membrane, clinical data regarding the silk membrane has been limited. However, silk based material has been used clinically as vessel-tie material and an electrospun silk membrane was applied successfully to patients. No adverse effect related to the silk suture has been reported. Considering that silk membrane can be provided to patients at a cheap price, its clinical application should be encouraged.

Key words: Membrane, Bone, Silk, Collagen, Polymer

Introduction

In recent decades, guided bone regeneration (GBR) procedures have been commonly performed to repair bone defect due to pathologic lesions or to augment alveolar bone for dental implant treatment[1]. In the GBR procedure, the role of barrier membrane is crucial for proper bone regeneration. It can prevent in-growth of soft tissue to the bone defect, and maintain the defect space during bone tissue regeneration. To achieve maximum bone regeneration, GBR membrane should have several characteristics, including (1) biocompatibility; (2) proper stiffness for space maintenance; (3) prevent epithelial cell migration; and (4) appropriate resorption time after proper bone regeneration[2].

Many tissue engineering studies have been conducted for development of an ideal GBR membrane from various natural and synthetic sources. Clinically, collagen membrane and expanded polytetrafluoroethylene (ePTFE) membrane have been widely used for the GBR procedure. Numerous clinical studies with these membranes have demonstrated their clinical usefulness. However, these membranes still have limitations in terms of ideal characteristics of GBR membrane.

In the clinical aspect, the indications for GBR membrane have increased, GBR membrane has mainly been used for bone augmentation surgery[3]. Recently, GBR membrane has been used for mandibular third molar extraction[4] or...
periodontal flap surgery[5]. GBR membrane is also used for treatment of peri-implant bone loss[6]. Although the indications for GBR membrane have increased, its clinical application has not shown a rapid increase. The main obstacle for its wide clinical application may be its high price. In this article, commercially available GBR membranes are selectively reviewed. In addition, silk materials are reviewed as GBR membrane. The limitations of each material and the future perspective are also discussed.

Collagen

Collagen membrane is a representative absorbable GBR membrane. Commercially available membranes are shown in Table 1. Collagen, the major constituent of connective tissue, is a structural component. It showed excellent biocompatibility when applied in tissue engineering[7]. Type I and III collagens derived from porcine, bovine, and human were mainly used in production of GBR membrane[8]. Thus, its antigenicity should be eliminated through specific chemical processes.

Rapid degradation is another disadvantage of collagen materials. To overcome rapid degradation, cross-linking treatments using glutaraldehyde, formaldehyde, or enzyme were performed depending on commercial products[9,10], which can control the absorption times of the collagen membrane during the bone regeneration period. However, some fixatives, such as glutaraldehyde, can be cytotoxic[11]. In general, the surface of collagen membrane is modified for acceleration of tissue integration (Fig. 1).

In clinical use, collagen membrane generally has less stiffness compared with non-absorbable membrane such as ePTFE or titanium mesh[12]. Thus, the space maintaining ability was lower than that of ePTFE or titanium mesh. The collagen membrane can be used for labial or buccal bone augmentation procedure combined with autogenous block bone graft[13]. Therefore, the bone graft has frequently accompanied the collagen membrane application during the GBR procedure[14]. The complication ratio of

![Fig. 1. Scanning electron microscopic view of collagen membrane.](image-url)

**Table 1. Summary of commercially available membrane for guided bone regeneration**

| Product          | Manufacturer          | Biodegradation | Crosslinking                       | Raw materials                        |
|------------------|-----------------------|----------------|------------------------------------|---------------------------------------|
| AlloDerm         | BioHorizons           | Yes            | Not presented                      | Acellular dermal matrix human skin    |
| Bio-Arm          | ACE Surgical Supply   | Yes            | Not presented                      | Porcine type I collagen               |
|                  | Company               |                |                                    |                                       |
| Bio-Gide         | Geistlich             | Yes            | No                                 | Porcine type I, III collagen           |
| Biomed           | Zimmer Dental        | Yes            | Yes (glutaraldehyde crosslinking)  | Bovine type I collagen                |
| Cytoblast RTM collagen | Osteogenics Biomedical | Yes           | Not presented                      | Bovine type I collagen                |
| Guidoss          | Nibeck                | Yes            | Yes                                | Porcine type I collagen               |
| OSSiX plus       | OraPharma             | Yes            | Yes (sugar based crosslinking)     | Porcine-based collagen                |
| OsseeGuard Flex  | BIOMET 3i             | Yes            | Yes                                | Bovine type I, III collagen           |
| EZCure           | Biomatante            | No             | No                                 | Porcine-based collagen                |
| Lyoplant         | B. Braun Melsungen AG| Yes            | Yes                                | Bovine collagen                       |
| Rapiderm         | Dalim medical         | Yes            | Not presented                      | Porcine type I collagen               |
| Rapigide         | Dalim medical         | Yes            | Not presented                      | Porcine type I collagen               |
| Surederm         | Hans GBR              | Yes            | Not presented                      | Human skin tissue                     |
| Cytoflex (open membrane TEF guard) | Unicare biomedical | No             | No                                 | Micro- porous, PTFE membrane          |
| Cytoplast (Ti-250 or Ti-150 Titanium-Reinforced) | Osteogenics biomedical | No | No | High-density PTFE membrane |
| Cytoplast TXT200 | Osteogenics biomedical | No | No | High-density PTFE membrane |
| Gore-TEX         | W. L. Gore and Associates | No | No | ePTFE membrane |
| Open-tex         | Purgo                 | No             | No                                 | High-density PTFE (100%) membrane     |

PTFE, polytetrafluoroethylene; ePTFE, expanded polytetrafluoroethylene.
the collagen membrane has been lower in the GBR procedure. Premature exposure of the collagen membrane shows severely compromised amounts of bone regeneration[15].

**Synthetic Polymers**

Aliphatic polyesters such as polylactic acid (PLA), polyglycolic acid (PGA), poly(ε-caprolactone), and polydioxanone have been used for production of synthetic polymers[16]. Synthetic polymers have traditionally been used for the plate and screw systems in orthopedic surgery[17]. In dentistry, the PLA membrane was first used for periodontal tissue regeneration[18]. After that, various GBR membranes, for example, Guidor (Sunstar Americas Inc, Chicago, IL, USA), Resolut (W.L. Gore & Associates Inc., Newark, NJ, USA), Atrisorb (Atrix Laboratories Inc., Fort Collins, CO, USA), Epi-Guide (Kensey Nash Corp., Research Triangle Park, NC, USA), and Biomesh (Samyang Corp., Seoul, Korea) have been commercially available.

The PLA polymer showed a slower hydrolysis rate compared with the PGA polymer in the human body[19]. For proper degradation of polymer, PLA polymer has mainly been combined with the PGA polymer as a copolymer; these polymers degrade by enzymatic hydrolysis[20]. Thus, Poly(lactic-co-glycolic) acid (PLGA) has mainly been used in dentistry for synthesis of GBR membrane[21]. The compositional change of PLGA affects the hydrolysis rate and mechanical strength of the GBR membrane[22]. Synthetic polymer membranes showed less inflammation when applied in the GBR procedures[23]. In addition, it can also be used as a carrier for drug delivery[24]. Compared to collagen membrane, when using the synthetic polymer membrane, there is no possibility of cross infection and less limitation of its production. As most synthetic polymer is poorly bio-degradable, it should be removed after bone regeneration. Synthetic polymer is usually encapsulated by the fibrotic capsule[25]. Without incorporating bio-active molecules, synthetic polymer membrane itself does not have osteoinduction ability[26]. Therefore, compared to collagen membrane, new bone formation in the bony defect was lower[12].

Among the synthetic polymers, ePTFE has been widely used as a GBR membrane (Fig. 2). The ePTFE membrane is used with autogenous bone grafting for GBR[27]. In cases of autogenous bone grafting, premature exposure of ePTFE membrane does not influence the clinical outcome[27]. Immediate implant installations after tooth extraction and augmentation with ePTFE membranes have predictable results[28]. However, contamination of ePTFE membrane has shown unfavorable results. Infection is a serious risk factor for arterio-venous PTFE grafts[29]. The extent of bacterial contamination of the ePTFE membrane is an indicator of the long-term success of the GBR procedure[30].

**Silk**

Silk, a macromolecule produced by *Bombyx mori*, has...
been used as a suture material in the medical field for a long time[31]. In particular, silk fibroin, a structural protein of silk material, has high biocompatibility and less foreign body reaction[32]. Silk fibroin has a fibrous structure and sericin is an adhesive for the silk fibroin. Silk fibroin has been investigated as a scaffold for bone grafts[33], artificial dura[34], wound dressing[35], or vessel[36]. Among commercialized silk-based materials, there is artificial tympanic membrane[37].

Silk fibroin usually induces a foreign body reaction when it is implanted into the bone defect (Fig. 3). If the silk fibroin is degraded by acid treatment, its molecular weight can be decreased below 1 kDa[38]. This low molecular weight silk protein can increase alkaline phosphatase activity and collagen synthesis in MG63 cells[38]. Use of this low molecular weight silk protein with platelet-rich-fibrin can increase bone regeneration in the rabbit calvarial defect model[39] and peri-implant bone defect model[40]. Silk membrane has not been commerciallyized for the GBR procedure. However, several recent studies have reported on its potential application as a membrane for the GBR procedure[41-44].

Silk membrane can be produced by different methods of methods, including electrospun technique[44], casting technique[41,43], and simple separation technique[45]. Regardless of the production method, silk fibroin membrane showed favorable bone regeneration and less inflammation in the rat or rabbit calvarial defect model[41-45]. Electrospun silk membrane for the GBR technique was introduced by a team at Seoul National University in 2005[44]. The electrospun technique is proper for use in mass production (Fig. 4). In testing for patients it showed generally acceptable results[46,47]. However, the setting up and operating cost for the electrospun facility was higher than that for collagen membrane production (data not shown).

Silk membrane can be produced by casting technique[41,43]. Using this technique, a transparent silk membrane can be produced[43]. Similar technique has been used for production of the artificial tympanic membrane[48]. When compared to the unfilled control, this film type membrane showed higher new bone formation[43]. The silk membrane is surrounded by thin fibrotic tissue and very low inflammatory reaction around the silk membrane (Fig. 5). However, it is brittle in dry state. In wet condition, it has very low suture tensile strength. Therefore, the vacuum package is required to prevent breakage of the membrane. Although this film type membrane can be produced at two thirds the price of the available collagen membrane, the handling difficulty may be an obstacle to its wide application.

Recently, silk membrane is produced by a simple separation method[45]. The cocoon of *Bombyx mori* has a multi-layered structure[49]. These layers can be separated by shear stress. The thickness of the separated layer can generally range from 0.02 to 0.5 mm[49]. Separated layer has a thin fibrous network (Fig. 6). In dry condition, the silk membrane has similar tensile strength to the collagen membrane (Fig. 7). However, the tensile strength of this silk
membrane is higher than that of collagen membrane or ePTFE membrane in wet state[45]. New bone formation is also comparable to that of collagen membrane[45]. In a previous report, PLGA barrier membrane did not show statistically greater new bone formation than negative control, but the collagen membrane did[50]. Silk membrane and collagen membrane show higher new bone regeneration compared to ePTFE membrane[45]. Foreign body giant cells were observed around the silk membrane, but the inflammatory reaction was minimal and new bone formation was observed below the silk membrane (Fig. 8). Unlike other collagen membranes, this silk membrane can be stored at room temperature. It can be sterilized by ethylene oxide gas, autoclave, or irradiation (data not shown). Thus, overall production cost will be much lower than that of other types of membrane. However, there has been no data on its clinical application.

In addition, silk is an excellent drug carrier. Several candidate drugs can be incorporated into the silk membrane. Antiseptic drugs such as tetracycline[51] and 4-hexylresorcinol (4HR)[42] were combined on the silk membrane for better bone regeneration. Tetracycline has been incorporated into other types of grafts. Tetracycline incorporated bone graft materials generally showed more bone formation than those without[52,53]. As tetracycline can hold the calcium ion, localized free calcium ion can be elevated in the presence of tetracycline. It can activate osteoblast and new bone formation[54]. 4HR is a chemical chaperone and a dormancy inducer for the microorganism[55]. 4HR inhibits transglutaminase-2[56] and nuclear factor-κB pathway[57]. 4HR can also inhibit calcium oscillation[58] and diacylglycerol kinase pathway[59]. Therefore, 4HR may activate osteoblast and macrophage. 4HR incorporated dental implant[60] or bone graft[61] showed higher bone formation, but its action is dose-dependent, 4HR also accelerates the bio-degradation of grafts[59]. If silk membrane should be degraded within a couple of weeks, 4HR incorporated silk membrane may be used.

Commercialization of Silk Membrane

In recent decades, silk materials have been widely stud-
ied for dental and medical application. However, only film type silk membrane has been approved as a substitute for the tympanic membrane by the Korean Food and Drug Administration. In addition, the silk tympanic membrane is not widely used due to the imbalance between the cost for production and the price suggested by the health insurance. In the case of the tympanic membrane, most patients are healed naturally without artificial membrane. Only severely injured patients may need the artificial tympanic membrane. Therefore, its clinical application may be limited.

Unlike the silk tympanic membrane, silk membrane produced by simple separation method does not require the degumming process. Therefore, there was no risk of residual bio-hazard salts that were added during the degumming process. However, separation itself should be done manually; it was very labor intensive work. The size of the silk membrane produced by simple separation is dependent on the cocoon size. Therefore, a large sized membrane cannot be produced by use of this technique. Thus, this silk membrane cannot be used for covering maxillary sinus wall defect or cystic cavity wall defect. Despite these limitations, this new silk membrane can be widely used for covering small sized intra-oral defect such as extraction socket, periodontal defect, and peri-implant defect. As the silk material is classified as a non-biodegradable material, the clinical method for the silk membrane is generally in accordance with that of small sized ePTFE membrane. Compared to vessel tie silk material, the silk membrane for GBR, located mainly in the submucosal layer, can be easily removed. Whether it can be used for an open-membrane technique like collagen membrane is not clear. It should be tested in the clinical application.

Conclusion

There have been numerous patients who potentially need the GBR membrane. However, the cost for using the membrane is a main obstacle for its wide applications. When the silk membrane produced by simple separation method is commercialized, its price will be much lower than that of any other currently available types of membrane. Development of better material is a vital component of public health care.

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References

1. Nguyen TT, Mui B, Mehrabzadeh M, et al. Regeneration of tissues of the oral complex: current clinical trends and research advances, J Can Dent Assoc 2013;79:41.
2. Rakhmatia YD, Ayukawa Y, Furushashi A, Koyano K. Current barrier membranes: titanium mesh and other membranes for guided bone regeneration in dental applications, J Prosthodont Res 2013;57:3-14.
3. Khajasteh A, Morad G, Behnia H. Clinical importance of recipient site characteristics for vertical ridge augmentation: a systematic review of literature and proposal of a classification, J Oral Implantol 2013;39:386-98.
4. Corinaldesi G, Lizio G, Badiali G, Morelli-Labate AM, Marchetti C. Treatment of intra-bony defects after impacted mandibular third molar removal with bioabsorbable and non-resorbable membranes, J Periodontol 2011;82:1404-13.
5. Cortellini P, Tonetti MS. Clinical performance of a regenerative strategy for intra-bony defects: scientific evidence and clinical experience, J Periodontol 2005;76:341-50.
6. Schwarz F, Hegewald A, Sahm N, Becker J. Long-term follow-up of simultaneous guided bone regeneration using native and cross-linked collagen membranes over 6 years, Clin Oral Implants Res 2014;25:1010-5.
7. Chattopadhyay S, Raines RT. Review collagen-based biomaterials for wound healing, Biopolymers 2014;101:821-33.
8. Parrish LC, Miyamoto T, Fong N, Mattson JS, Cerutis DR. Non-bioabsorbable vs. bioabsorbable membrane: assessment of their clinical efficacy in guided tissue regeneration technique, A systematic review, J Oral Sci 2009;51:383-400.
9. Verissimo DM, Leitão RF, Ribeiro RA, et al. Polyanoionic collagen membranes for guided tissue regeneration: effect of progressive glutaraldehyde cross-linking on biocompatibility and degradation, Acta Biomater 2010;6:4011-8.
10. Rothamel D, Schwarz F, Sager M, Herten M, Sculean A, Becker J. Biodegradation of differently cross-linked collagen membranes: an experimental study in the rat, Clin Oral Implants Res 2005;16:369-78.
11. Speer DP, Clavaplí M, Eskelson CD, Urelec J. Biological effects of residual glutaraldehyde in glutaraldehyde-tanned collagen biomaterials, J Biomed Mater Res 1980;14:753-64.
12. Caffesse RG, Nasjleti CE, Morrison EC, Sanchez R. Guided tissue regeneration: comparison of bioabsorbable and non-bioabsorbable membranes, Histologic and histometric study in dogs, J Periodontol 1994;65:580-91.
13. Proussefs P, Lozada JL. The use of resorbable collagen membrane in conjunction with autogenous bone graft and inorganic bovine mineral for buccal/labial alveolar ridge augmentation: a pilot study, J Prosthodont 2003;9:530-8.
14. Urban IA, Jovanovic SA, Lozada JL, Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical
scenarios prior to implant placement: a retrospective study of 35 patients 12 to 72 months after loading, Int J Oral Maxillofac Implants 2009;24:502-10.

15. Bornstein MM, Bosshardt D, Buser D. Effect of two different bioabsorbable collagen membranes on guided bone regeneration: a comparative histomorphometric study in the dog mandible. J Periodontol 2007;78:1943-53.

16. Zhao L, Li N, Wang K, Shi C, Zhang L, Luan Y. A review of polyepptide-based polymersomes, Biomaterials 2014;35:1284-301.

17. Roldaen A. Absorbable materials in orthopaedic surgery, Ann Med 1991;23:109-15.

18. Galgut P, Pittrolo R, Waite I, Doyle C, Smith R. Histological evaluation of biodegradable and non-degradable membranes placed transcutaneously in rats, J Clin Periodontol 1991;18:581-6.

19. Daniels AU, Andriano KP, Smutz WP, Chang MK, Heller J. Evaluation of absorbable polylactic(ortho esters) for use in surgical implants, J Appl Biomater 1994;5:51-64.

20. Antronissau KA, Agrawal GM, Barber FA, Burkheart SS. Orthopaedic applications for PLA-PGA biodegradable polymers, Arthroscopy 1998;14:726-37.

21. Urakami K, Higashi A, Umemoto K, Godo M, Watanabe C, Hashimoto K. Compositional analysis of copoly (DL-lactic/glycolic acid) (PLGA) by pyrolysis-gas chromatography/mass spectrometry combined with one-step thermally assisted hydrolysis and methylation in the presence of tetracethylammonium hydroxide. Chem Pharm Bull (Tokyo) 2001;49:203-5.

22. Jones AA, Buser D, Schenk R, Wozney J, Cochran DL. The use of a silk fibroin membrane for the guided bone regeneration in rats, J Neurosurg 2011;114:485-90.

23. De Stefano D, De Rosa G, Maimi MC, et al. Oligonucleotide decoy to NF-kappaB slowly released from PLGA microspheres reduces chronic inflammation in rat, Pharmacol Res 2009;60:35-40.

24. Lee SW, Kim SY, Song JY, et al. Silk fibroin and 4-hexylresorcinol incorporation membrane for guided bone regeneration, J Craniofac Surg 2013;24:1927-30.

25. Lee EH, Kim JH, Kweon HY, et al. A combination graft of low-molecular-weight silk fibroin with Choukroun platelet-rich fibrin for rabbit calvarial defect, Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:e33-8.

26. Jang ES, Park JW, Kweon H, et al. Restoration of peri-implant defects in immediate implant installations by Choukroun platelet-rich fibrin and silk fibroin powder combination graft, Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:831-6.

27. Lee SW, Kim SG, Song JY, et al. Silk fibroin and 4-hexylresorcinol incorporation membrane for guided bone regeneration, J Craniofac Surg 2013;24:1927-30.

28. Beckers W, Dallin C, Lehnhom U, et al. Five-year evaluation of implants placed at extraction and with dehiscences and fenestration defects augmented with ePTFE membranes: results from a prospective multicenter study, Clin Implant Dent Relat Res 1999;1:27-32.
and polytetrafluoroethylene membrane for guided bone regeneration, Macromolecular Res 2014;22:475-82.
46. Han DH, Hong KS, Chung CH, Yim SB. A comparative study for guided bone regeneration of silk fibroin nano-
membrane(NanoGide-S(TM)). J Korean Acad Periodontol 2008;39:129-38.
47. Hwang WJ, Jeong SN, Kim YS, et al. Clinical study of guided bone regeneration of extracted socket with PLA/PGA mem-
brane and silk fibroin membrane. J Korean Acad Periodontol 2009;39:129-38.
48. Kim J, Kim CH, Park CH, et al. Comparison of methods for the repair of acute tympanic membrane perforations: Silk patch vs. paper patch. Wound Repair Regen 2010;18:152-8.
49. Zhang J, Kaur J, Rajkhowa R, Li JL, Liu XY, Wang XG. Mechanical properties and structure of silkworm cocoons: a comparative study of Bombyx mori, Antheraea assamensis, Antheraea pernyi and Antheraea mylitta silkworm cocoons. Mater Sci Eng C Mater Biol Appl 2013;33:3206-13.
50. Sommerlad S, Mackenzie D, Johansson C, Atwell R. Guided bone augmentation around a titanium bone-anchored hear-
ring aid implant in canine calvarium: an initial comparison of two barrier membranes. Clin Implant Dent Relat Res 2007;9:
22-33.
51. Lee SW, Park YT, Kim SG, et al. The effects of tetracycline-loaded silk fibroin membrane on guided bone regeneration in a rabbit calvarial defect model. J Korean Assoc Maxillofac Plast Reconstr Surg 2012;34:293-8.
52. Dashti A, Ready D, Sulli V, et al. In vitro antibacterial efficacy of tetracycline hydrochloride adsorbed onto Bio-Oss bone graft. J Biomed Mater Res B Appl Biomater 2010;93:394-400.
53. Harris RJ. Treatment of furcation defects with an allograft-alloplast-tetracycline composite bone graft combined
with GTR: human histologic evaluation of a case report. Int J Periodontics Restorative Dent 2002;22:381-7.
54. Gomes PS, Santos JD, Fernandes MH. Cell-induced response by tetracyclines on human bone marrow colonized hydroxy-
apatite and BoneLike. Acta Biomater 2008;i:630-7.
55. Kozubek A, Tyman JH. Resorcinolic lipids, the natural non-isoprenoid phenolic amphiphiles and their biological
activity. Chem Rev 1999;99:1-26.
56. Kim SG, Jeong JH, Park YW, et al. 4-Hexylresorcinol inhibits transglutaminase-2 activity and has synergistic effects along with cisplatin in KB cells. Oncol Rep 2011;25:1597-602.
57. Kim SG, Lee SW, Park YW, Jeong JH, Choi JY, 4-hexylresorcinol inhibits NF-κB phosphorylation and has a synergistic effect with cisplatin in KB cells. Oncol Rep 2011;26:
1527-32.
58. Kim SG, Choi JY, 4-hexylresorcinol exerts antitumor effects via suppression of calcium oscillation and its antitumor
effects are inhibited by calcium channel blockers. Oncol Rep 2013;29:1835-40.
59. Kweon H, Kim SG, Choi JY. Inhibition of foreign body giant cell formation by 4-hexylresorcinol through suppress-
persion of diacylglycerol kinase delta gene expression. Biomaterials 2014;35:8576-84.
60. Kim SG, Hahn BD, Park DS, et al. Aerosol deposition of hydroxyapatite and 4-hexylresorcinol coatings on titanium alloys for dental implants. J Oral Maxillofac Surg 2011;69:e354-63.
61. Kim MK, Park YT, Kim SG, Park YW, Lee SK, Choi WS. The effect of a hydroxyapatite and 4-hexylresorcinol combination graft on bone regeneration in the rabbit calvarial defect model. J Korean Assoc Maxillofac Plast Reconstr Surg 2012;34:
377-83.