PC 2. Unexpectedly, however, in this study, the nearest odor to BR was DE, and the farthest odor was TC.

This relation between the odors may be caused by characteristic of the denture. The subjects in this study were elderly persons (over 70 years old). It is reported by Hoad-Reddick [17] that only 40% of the dentures of the elderly are properly cleaned. In this study, the subjects' denture hygiene was not assessed, but they may have not cleaned their dentures properly. It is recommended that dentures should be cleaned mechanically and to use denture cleaner after mechanical cleaning. But even though dentures are cleaned properly, the sterilization of dentures are effective in only few denture cleaners [18].

Tanaka [19] reported that the responses of the e-nose, which was the same type as that used in this study had positive correlations with age, smoking habits, pocket depth, tongue coating status, and plaque score. VSC concentrations of the breath showed positive correlations with only tongue coating status and plaque score. Tanaka's findings indicate that the e-nose is capable of detecting of not only VSC but also other gases. It is suggested that gases beside VSC may affect the similarity of BR and DE, which comes from the PC 1 result.

Previous findings show that tongue coating is the main cause of breath odor [2, 15, 16]. However, there have been no reports referring to the characteristics of BR and TC due to a lack of an objective method for discriminating the odor characteristics. Moreover, odor characteristics determined by human judges may lack objectivity, and the outcome of the organoleptic judgment may not be reproducible.

This electronic nose system is regarded as the objective method for discriminating odor characteristics. In spite of the previous reports that BR and TC are similar, the results of PCA and of one-way ANOVA clearly separated the two odors. From the present results, it cast doubt on the view that the tongue coat is the main cause of breath odor in the elderly patients. In previous studies [11, 12], the age distribution of the subjects tends to be younger than the subjects in this study. The results of this study do not contradict the fact that the tongue coat is the main cause of breath odor in the younger population. However, in the elderly, denture odor can be assumed to have a closer relation to breath odor.

Conclusion

The tongue coat odor, previously named as the main cause of breath odor, had no similar characteristics to breath odor. In the elderly, odor from the denture could be insisted to have a closer relation to breath odor.

Acknowledgments

This research was supported in part by a Health Science Grant (H16-iryou-020) from the Ministry of Health, Labour and Welfare, Japan. We thank Yoshie Usui, MS, for manuscript preparation. This research was presented in part as a poster at the 52nd annual meeting of Japanese Association for Dental Research, Tokyo, November 27-28, 2004.

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高齢者の口臭と口腔内のにおい発生源の関連
—電子嗅覚装置の測定結果より—

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抄録：高齢者の口臭と口腔内のにおい発生源となる唾液，使用中の義歯，舌苔のにおいを比較し，相互のにおいの関係を明らかにすることを目的とした。我々の勤務する歯学部付属病院の外来受診患者を対象とした。対象患者の口臭，唾液，舌苔および義歯を採取し，各々の揮発ガスをサンプリングバッグに集めた。サンプルガスは電子嗅覚装置（におい識別装置FF-1，島津製作所）を用いて測定した。においのデータ解析には主成分分析を用いた。口臭と口腔内のにおい発生源（唾液，舌苔，使用中の義歯）の比較には1元配置の分散分析を用いた。多重比較にはSchefféテストを行った。第一主成分で口臭と唾液，口臭と義歯，口臭と舌苔のにおいには有意な差が認められた（$p<0.001$）。唾液と舌苔（$p=0.554$），唾液と義歯（$p=0.526$），舌苔と義歯（$p=0.074$）間のにおいには有意な差を認めなかった。口臭，唾液，舌苔，義歯，それぞれに対する平均値の差の比較では口臭に一番近いのは義歯，次いで唾液，最後に舌苔となっていた。本研究では高齢者においては舌苔のにおいはむしろ唾液のにおいと類似した傾向があることが明らかになった。高齢者の口臭のにおい発生源としては義歯が関連が深いことが明らかになった。

キーワード：口臭，高齢者，電子嗅覚装置

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An ingenious design for peptide vaccines

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Available online 21 January 2005

Abstract

For humoral immunization, it may be possible to make effective and safe peptide vaccines for various diseases by selection of proper B-cell epitopes. However, a lack of T-cell epitopes on short peptides, such as those associated with major histocompatibility complex (MHC)-restriction, is a major problem for peptide vaccine development. We propose a solution for the design of peptide vaccines that involves induction of broadly reactive T-cell epitopes via agretopes. The strategy involves positioning multi-agretope type peptides on the N-terminal side of a di-lysine linker and B-cell epitopes on the C-terminal side. The addition of the arginine–glysine–aspartate (RGD)-motif to the N terminus of the peptide enhances its immunogenicity, and enables nasal immunization without adjuvants.

Keywords: RGD-motif; Multi-agretope; MHC-restriction

1. Introduction

The advantage of a peptide vaccine is that it can induce immune responses to a specific sequence of amino acids. However, the vaccine peptide must contain at least one major histocompatibility complex (MHC) binding motif (agretope) as an antigen, since antigens are presented by the immune system as a short peptide that binds to the MHC. Subsequently, the T-cell receptors recognize the peptide as a T-cell epitope on the MHC molecules [1–3]. For a humoral immune response, a peptide must have B-cell epitopes to induce specific antibodies and at least one agretope/T-cell epitope for presentation by MHC class II (MHC-II) molecules [1–3]. However, there are over 10 haplotypes of MHC-II in human [1] and the agretopes are different for each haplotype. The MHC-restriction is the most critical impediment to the development of peptide vaccines.

A peptide vaccine has another disadvantage. The weak antigenicity of peptide vaccines dictates a need for use of strong adjuvants, such as Freund's, for induction of antibodies. Several approaches, such as liposome capsulation [4], MAPs [5], and lipopeptides [6] have been used to eliminate the need for strong adjuvants. We have introduced the arginine–glysine–aspartate (RGD)-motif into peptide antigens. The RGD-motif is the most representative cell attachment motif seems to enhance the binding of peptides to specific receptors. Antigenicity of the peptides was enhanced and nasal immunization by peptides was successful without adjuvants [7].

We have proposed a design for peptide vaccines that contain the RGD-motif, and the lysine linker (-KK-) that joins two peptides [7,8]. The lysine linker is the target sequence of the lyzosomal protease, cathepsin B, which is one of the important proteases for antigen processing in the context of MHC-II antigen presentation [2]. When two peptide antigens are joined with -KK-, we can avoid induction of antibodies to the amino acid sequence that is generated by joining of two peptides and most antibodies are reactive to each peptide [8]. In our previous report, we have noticed a bias between the peptides, depending upon whether they are on the N- or C-terminal side of -KK- for induction of antibodies [7]. In this study, we have investigated the reason for this bias and pro-

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doi:10.1016/j.vaccine.2005.01.031

pose the use of the bias as a solution to the MHC-restriction problem.

2. Materials and methods

2.1. Peptide synthesis

All peptides used in this study were synthesized by a stepwise solid-phase procedure as described previously [7]. Peptides were verified by MALDI-TOF/MS (Voyager-DE^{TM}S TR work station: Applied Biosystems Foster City, CA) when necessary. The single-letter universally accepted notation for amino acids is used throughout the text.

2.2. Immunizations

BALB/c, B10.D2, B10.S, B10.A, and C3H/HeJ mice were obtained from Japan SLC Inc. (Shizuoka, Japan) and were used at 6 weeks of age to begin the immunization in all experiments. Groups of four to six mice were immunized intranasally with 50 μg of a peptide, either with or without 1 μg of cholera toxin (CT: Sigma-Aldrich, Missouri). A micropipettor was used to gently instill 4 μL of immunogen-containing saline solution into the nasal cavities of each mouse (2 μL into each nasal orifice). Two identical booster doses were given at 2-week intervals.

One group of mice was primed subcutaneously with 100 μg of peptides in 100 μL phosphate-buffered saline (PBS) either with or without 100 μL Freund's incomplete adjuvants (FIA: Pierce and Endogen: Funakoshi Co. Ltd., Tokyo, Japan). The same subcutaneous booster dose was given at 2-week intervals.

HA vaccine (split-product virus vaccine) was prepared from influenza virus A/PR/8/34 (A/PR8, H1N1) according to the method of Davenport et al. [9] at the Kitasato Institute (Saitama, Japan). Groups of BALB/c mice were intranasally immunized 1 μg of HA vaccine with 1 μg of peptide or 1 μg of CT. Four booster doses were given at 2-week intervals.

One week after the last booster dose, animals were bled and serum samples were prepared from clotted blood by centrifugation and stored individually with Complete^{TM} protease inhibitor cocktail (Roche Diagnostics Japan, Tokyo) and 0.05% (w/v) of sodium azide.

2.3. ELISA assays

Protein antigens used for ELISA were BSA, OVA, and PAc. Recombinant PAc was isolated from *Streptococcus mutans* TK18 as described previously [10]. For the ELISA, 96-well microtiter H-plates (Sumitomo Bakelite, Tokyo, Japan) were coated with 2 μg/well peptide or 1 μg/well protein antigen in 100 μL of 50 mM carbonate buffer pH 9.6 and held overnight at 4 °C. All assays were performed with alkaline phosphatase and *p*-nitrophenyl phosphate systems as described previously [7]. The $OD_{405-620}$ was measured using a microtiter plate reader (Multiskan BICHROMATIC, Labosystem, Helsinki, Finland). The ELISA antibody titer was expressed as the reciprocal of the highest dilution giving an $OD_{405-620}$ of 0.1 unit above that of the control wells without antigen.

3. Results and discussion

3.1. Investigation of B-cell epitopes

SmU, with the amino acid sequence TYEAALKQYEADL, is a minimum peptide antigen (PAc365–377) for the induction of antibodies that cross react with the cell surface protein antigen of *S. mutans* [10]. SmU has both a strong B-cell epitope and the helper T-cell epitope for H-2^d haplotype mice, but lacks the T-cell epitope for H-2^s haplotype [11]. OVAp is a peptide antigen (OVA323–336: ISQAVHAAHAEINE) for induction of antibodies that are cross-reactive to ovoalbumin, which has strong epitopes for both B- and the T-cells of H-2^d haplotype mice [11]. To investigate the position bias of the peptide containing lysine linker, we synthesized the long peptides, SmU-KK-OVAp, OVAp-KK-SmU, RGD-SmU-KK-OVAp and RGD-OVAp-KK-SmU. We immunized mice both nasally and subcutaneously with the peptides, either with or without FIA. The serum titers to peptide antigens, PAc and OVA are shown in Fig. 1. In all cases, both SmU and OVAp were good antigens for BALB/c mice (H-2^d) and induced antibodies cross-reactive to PAc and OVA. When we focused on SmU, it was unclear whether the N- or C-terminal side of -KK- linker was the more favorable position for induction of antibodies to PAc. This was also true for OVAp. When the RGD-motif was added to the peptides

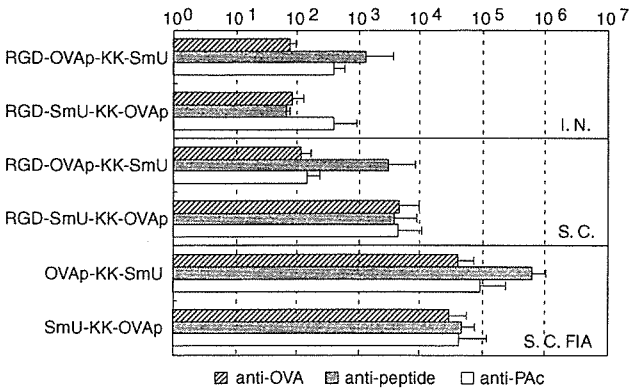

Fig. 1. Serum titres induced by intranasal and subcutaneous immunization with peptides. BALB/c mice were intranasally (I.N.) immunized with 50 μg of RGD added peptides, followed by two booster doses at two-week intervals. One hundred micrograms of peptide with FIA was used for subcutaneous (S.C.) immunization and immunization with RGD added peptides without adjuvant was followed by a booster dose given at a two-week interval. One week after the last booster dose, serum samples were collected and serum antibody titres were determined by ELISA. Average serum titers are shown for anti-OVA (hatched-box), anti-peptide antigen (grey-box) and anti-PAc (open box) with SD bars for each group.

and used for nasal immunization, SmU was a stronger antigen than OVAp, independent of its position. Those results clearly indicated that if both peptides, placed either on the N- or C-terminal side of -KK- linker, were strong enough as helper T-cell epitopes, antibody titers were dependent upon the strength of B-cell epitopes.

3.2. *The position of T-cell epitopes and MHC-restriction*

The effects of both the position and the strength of T-cell epitopes in the peptide, including the lysine linker, were examined. During the screening of SmU from the PAc, we had analyzed B- and T-cell epitopes of several peptides. PAc305–318 (NEADYQAKLTAYQT) has weaker B- and T-cell epitopes for H-2^d mice than SmU. However, unlike SmU, it has T-cell epitopes for H-2^s mice [11]. We have synthesized two peptides, SmU-KK-PAc305–318 and PAc305–318-KK-SmU that were used with FIA to subcutaneously immunize B10.D2 (H-2^d) and B10.S (H-2^s) mice (Fig. 2). B10.D2 mice responded with antibodies to both PAc305–318 and SmU in response to both peptides. SmU is a stronger B-cell epitope than PAc305–318, since anti-SmU titers are always higher than those of anti-PAc305-318. When we investigated the importance of the peptide position on either the N- or C-terminal side of the linker, the C-terminal position was best for induction of antibodies. B10.S mice produced antibodies only to the PAc305-318-KK-SmU. In this case, T-cell epitopes for H-2^s haplotype mice existed only on PAc305–318. Thus, we could conclude that T-cell epitopes should be placed on the N-terminal side of -KK- linker. The cause of this phenomenon is not clear. There may be molecular mechanisms that preferentially achieve MHC-II loading of peptides that are placed on the N-terminal side of the lyzosomal digestion site. Since SmU lacks T-cell epitopes for H-2^s haplotype, B10.S mice could not produce antibodies by immunization with SmU alone. However, we were able to induce antibodies to SmU by immunization with PAc305–318-KK-SmU.

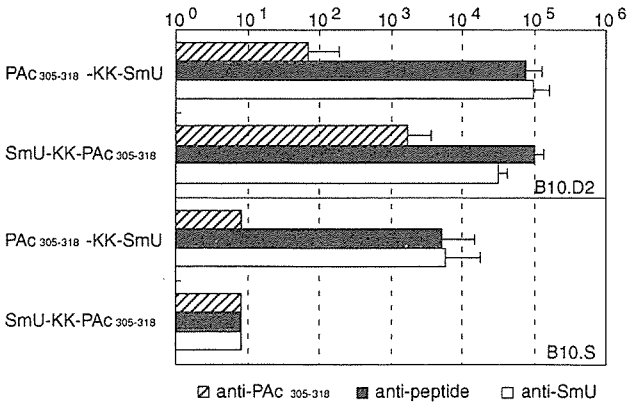

Fig. 2. Serum titres induced by subcutaneous immunization of peptides. B10.D2 and B10.S mice after subcutaneous immunization using peptides with FIA followed by a booster dose. Average serum titres are shown for anti-PAc305-318 (hatched-box), anti-peptide antigen (grey-box) and anti-SmU (open-box) with SD bars for each group.

This result shows a solution to MHC-restriction and points to the possibility of developing peptide vaccines for clinical use.

Thus, T-cell epitopes on the N-terminal side of -KK- linker were sufficient for induction of the antibodies. Therefore, if we placed the multi-agretope type peptide, broadly cross-reactive T-cell epitopes, such as T1 [12], Gag298-312 (KRWIILGLNKIVRMY)[13], or overlapping multi-agretope type peptide (OMP: LAVYWELLAKYLL-DRVQKVA) [7], on the N-terminal side of -KK- linker, we should be able to develop broadly effective peptide vaccines for human and verterinary use. However, peptides on the N-terminal side should not induce antibodies. We examined the ability of those peptides to induce antibodies by immunization of several types of mice. OMP and Gag298-312 with FIA were used to immunize B10.BR (H-2^k), B10.D2 (H-2^d), B10.S (H-2^s), BALB/c (H-2^d) and CH3/HeJ (H-2^k) mice and those peptides seemed to have very weak B-cell epitopes (Fig. 3A). Those peptides are suitable for T-cell epitopes in our peptide vaccines. We have synthesized peptides for induction of antibodies to SmU ((RGD-)OMP-KK-SmU) by immunization of B10.S mice (Fig. 3B). Intranasal immunization with OMP-KK-SmU alone did not induce specific antibodies because of its weak immunogenicity. Immunization with either RGD-added peptide alone or with CT induced

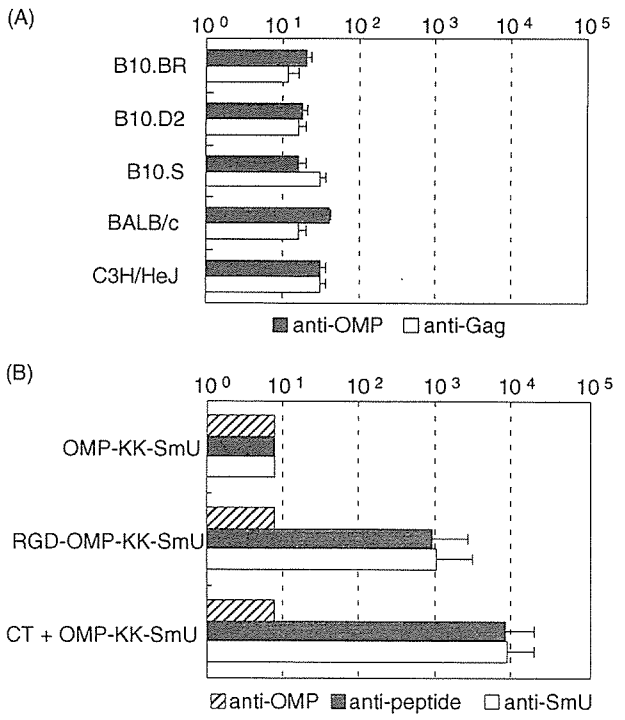

Fig. 3. Effect of multi-agretope type peptide on peptide antigens. (A) Each group of mice was immunized subcutaneously with FIA, followed by a booster dose, then specific antibody titres were determined by ELISA. Average titres are shown for anti-OMP (grey-box), and anti-Gag (open-box) with SD bars for each group. (B) B10.S mice were intranasally immunized either with or without CT. Average titres are shown for anti-OMP (hatched-box), anti-peptide antigen (grey-box), and anti-SmU (open-box) with SD bars for each group.

antibodies to SmU. OMP served as a T-cell for MHC-II of H-2^s mice in the same way as PAc305–318.

3.3. Application of the design of peptide vaccines

We have applied our design for peptide vaccines to an influenza vaccine. Several B-cell epitopes were reported that are involved in neutralization of the experimental strains of influenza virus A/PR8, HA1 (VTGLRNIPSIQSR) [14] and M2 (EVETPIRNEWGCRCNGSSD) [15]. We have synthesized peptide vaccines, RGD-Gag298-312-KK-HA1 and RGD-Gag298-312-KK-M2. In order to obtain high titer of antibodies, we immunized several mouse strains (data not shown) and B10.A was found to be the most reactive strain. Nasal immunization with peptides was repeated five times and serum titers were measured (Fig. 4A). In all cases, anti-HA1 and anti-M2 titers were specifically elevated. When two peptides were used for immunization at the same time, HA1 was a major antigen and when CT was used as mucosal adjuvant, M2 was major. It may be necessary to use additional approaches for the induction of antibodies to several peptides at the same time.

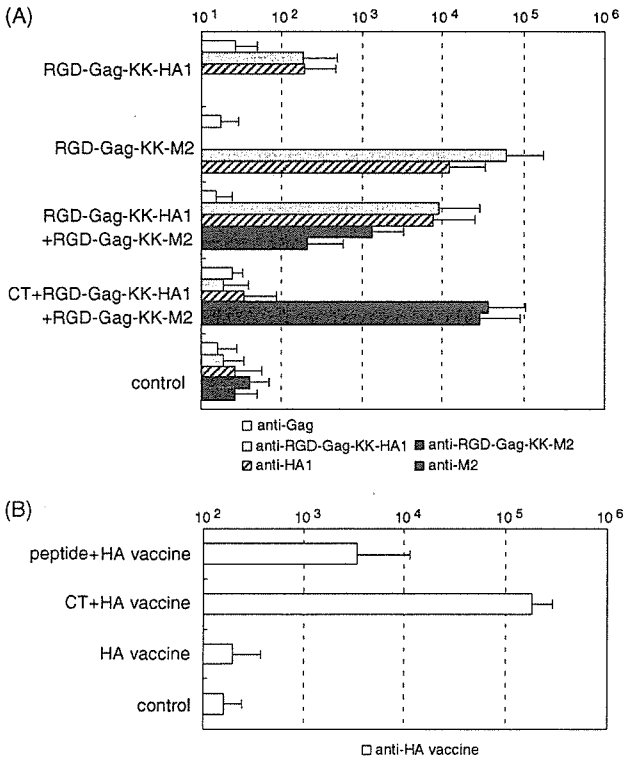

Fig. 4. Intranasal immunization with influenza vaccines. (A) B10.A mice were intranasally immunized with HA1 and M2 peptide vaccines, either with or without CT. Average titres are shown for anti-Gag (open-box), anti-HA1 (light grey-box), anti-RGD-Gag-KK-HA1 (hatched light grey-box), anti-M2 (dark grey-box) and anti-RGD-Gag-KK-M2 (hatched dark grey-box with SD bars for each group. (B) BALB/c mice were intranasally immunized with influenza HA vaccine (1 μg), with RGD-OMP-KK-OVAp (1 μg), or CT (1 μg), followed by four booster doses. Average anti-HA vaccine titres are shown as open-boxes with SD bars for each group.

Our peptide vaccines with the RGD-motif were reported as being useful adjuvants for nasal immunization [7]. When soluble proteins, such as BSA or OVA, were used for intranasal immunization with a small amount of RGD peptide vaccine, antibodies to BSA or OVA were strongly induced. However, background level antibodies to the RGD peptide were detected. In Fig. 4B, we have intranasally immunized mice using HA vaccines either with or without RGD peptide (RGD-OMP-KK-OVAp). The RGD peptide was already confirmed to be a nasal adjuvant in BALB/c mice [7]. After a series of five nasal immunizations, serum titers to HA vaccine were elevated by addition of the peptide, but the effects were weaker than when CT was added. In order to develop clinically useful peptide vaccines and adjuvants, we have to select for strong B-cell epitopes and develop the methods for enhancing the adjuvanicity of peptides.

In conclusion, our approach to the design of a peptide vaccine enables intranasal immunization without the need for adjuvant and solves the problem of MHC-restriction. Specifically, the design places the RGD at the N-terminus, a multiagretope peptide at the N-terminal side of lysine linker, and a B-cell epitope at the C-terminus. We suggest that our design might be universally applicable to the development of peptide vaccines and adjuvants for intranasal vaccination.

Acknowledgments

We would like to thank Ms Makiko Teramura-Hiramatsu, Ms Miho Sawada and Ms Yukiko Yamamoto for their assistance in performing the study. This work was supported by grants from the Ministry of Health, Labor and Welfare of Japan.

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Oral Diseases (2005) 11 (Suppl. 1), 35–36

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ORIGINAL ARTICLE

Clinical assessment of oral malodor intensity expressed as absolute value using an electronic nose

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OBJECTIVES: In our previous study, scores determined via a multiple linear regression method (EN-MLR) involving an electronic nose provided objective halitosis-related measurements; however, this model afforded only relative expression exclusively. The objective of this investigation was to assess clinically oral malodor intensity expressed as an absolute value using an electronic nose.

SUBJECTS AND METHODS: Sixty-six subjects were evaluated based on results of an actual organoleptic test (OLT), measurements of volatile sulfur compound (VSC) concentrations, a score representing malodor intensity (EN-MI) as the absolute value and EN-MLR measured with an electronic nose system. Oral health parameters were also examined.

RESULTS: The OLT score served as a benchmark. The area under the receiver-operating characteristic (ROC) plots of EN-MI score (0.975) was significantly larger than that of log VSC (0.896) ($P = 0.036$); however, the area did not differ significantly from that of EN-MLR score (0.932). Percentage of teeth with pocket depth ≥4 mm, tongue coating score and plaque control record displayed meaningful association with EN-MI score in multiple logistic regression analyses.

CONCLUSION: Oral malodor intensity expressed as an absolute value employing an electronic nose may be a suitable method for clinical evaluation of oral malodor.

Oral Diseases (2005) 11 (Suppl. 1), 35–36

Keywords: oral malodor; clinical assessment; electronic nose; oral health parameters

Introduction

The two primary methods applicable to clinical analysis of oral malodor are organoleptic test (OLT) and instrumental analysis, such as gas chromatography or use of a portable sulfide monitor (Rosenberg *et al*, 1991). However, since both techniques exhibit disadvantages, there remains no ideal objective approach for clinical assessment of the degree of oral malodor (Rosenberg, 1996). We previously reported that the scores determined with an electronic nose under top-note mode, provided objective halitosis-related measurements. However, those data were obtained via the multiple linear regression method (EN-MLR) and yielded relative rather than absolute values (Tanaka *et al*, 2004a). This investigation attempted to assess clinically oral malodor intensity expressed as an absolute value utilizing an electronic nose.

Subjects and methods

The subject population consisted of 46 individuals (mean age, 40.8 years) characterized by odor-judge ratings of ≥2.0 and 20 participants (mean age, 41.6 years) with odor-judge ratings of <2.0. Breath malodor was assessed with an electronic nose. Furthermore, volatile sulfur compound (VSC) measurements were conducted on a gas chromatograph; additionally, an OLT was performed.

The FF-1 odor discrimination analyzer (electronic nose, Shimadzu Ltd, Kyoto, Japan) utilized in the present study consisted of a preconcentrator, an array of six metal oxide semiconductor sensors selected for their distinct sensitivity and selectivity to fragrant substances, and pattern recognition software. The electronic nose was calibrated with nine standard gases including hydrogen sulfide, methylmercaptan, ammonia, trimethylamine, propionic acid, butylaldehyde, butylacetate, toluene and heptane (Shimadzu Ltd) before the measurement. The gas sample was introduced into the trap tube for 30 s, and then the trapped odor was driven to the sensor section with pure nitrogen. The odor spectrum was determined for nine categories of gases in the odor space formed by multiple output signals of sensors. The malodor intensity of sample gases as an absolute value was expressed as the vectorial sum of the malodor intensity of each category of gas (Kita *et al*, 2000). The score as a relative value was also obtained via a multiple linear regression method (Tanaka *et al*, 2004a). Probing depth was measured at two points

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around each tooth in all subjects and periodontal status was determined as a percentage of teeth displaying probing depth of ≥4 mm. O'Leary's plaque control records were also employed to assess oral hygiene status. In addition, tongue coating scores were determined by multiplying thickness by area (Tanaka *et al*, 2003).

Statistical comparisons of EN-MI, EN-MLR score and VSC level were analyzed using receiver-operating characteristic (ROC) plots with Rockit 0.9B Beta Version. Multiple linear regression and logistic regression analyses served to identify those oral health variables demonstrating a significant independent effect on EN-MI scores.

Results

Correlations between actual OLT score and EN-MI, EN-MLR scores or log total VSC derived from gas chromatography were examined. These three correlation coefficients were 0.81, 0.78 and 0.73, respectively. No meaningful difference was observed among the three correlation coefficients. ROC sensitivity-specificity plots afforded an appropriate protocol for comparison of EN-MI, EN-MLR scores and log total VSC data for classification of subjects with or without actual OLT score ≥2.0. Area under the ROC plots representing EN-MI scores (0.975) was markedly larger than that of log VSC (0.896) ($P = 0.036$); however, it did not differ significantly from that of EN-MLR (0.932) (Figure 1).

Logistic regression analyses were conducted which corresponded to the possibility of placement of subjects in the upper 25th percentile of EN-MI score distribution as a dependent variable. Percentage of teeth exhibiting probing depth of ≥4 mm, tongue coating score and plaque control record displayed significant association with EN-MI scores (odds ratios of 13.0, 7.1 and 28.2, respectively) ($P < 0.05$).

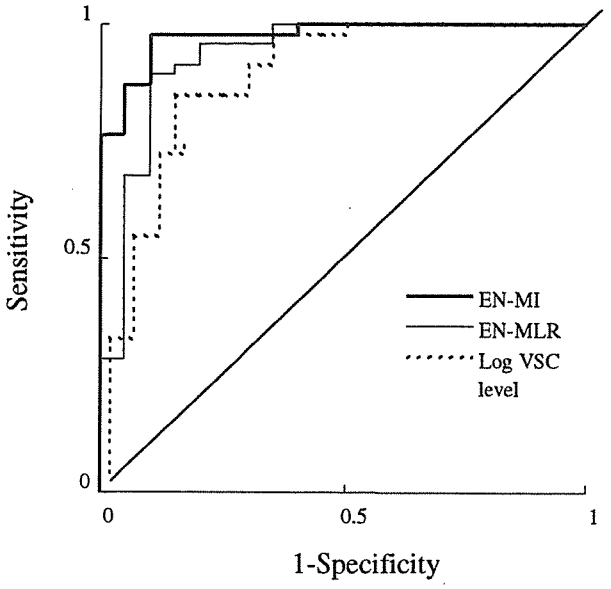

Figure 1 ROC plots comparing EN-MI, EN-MLR and log VSC data utilized for classification of subjects with or without OLT score of ≥2.0. Areas under ROC plots were 0.975 (EN-MI), 0.932 (EN-MLR) and 0.896 (log VSC)

Discussion

In the present investigation, EN-MI scores were compared with EN-MLR scores as oral malodor assessment employing an electronic nose system. The correlation coefficient between EN-MI score and OLT score ($r = 0.81$) was nearly identical to that between EN-MLR and OLT score ($r = 0.78$). Area under the ROC curve representing EM-MI score was also similar to that of EN-MLR; in contrast, it was significantly larger than that of log VSC. This finding suggests that EN-MI score determined with the electronic nose demonstrated a level of accuracy higher than that of log VSC for classification of subjects with or without actual OLT score of ≥2.0.

This study also established that EN-MI scores were independently correlated with periodontal health status, tongue coating and supra-gingival plaque accumulation. These results were consistent with those of EN-MLR scores (Tanaka *et al*, 2004a). We also previously reported that the periodontal pathogens on tongue dorsa contributed markedly to VSC production (Tanaka *et al*, 2004b). However, since the proportions of periodontal pathogens were weakly associated with OLT score, we suggested that other malodorous compounds in addition to VSC might also be related to OLT scores (Tanaka *et al*, 2004b). EN-MI may be attributed to various malodorous compounds which may be produced mainly at supra-gingival plaque, periodontal pocket and tongue coating. Thus, the relationship between amount of supra-gingival plaque, periodontal pocket depth and tongue coating and oral malodor may be effectively detected by EN-MI. We conclude that the absolute expression of malodor intensity with an electronic nose can afford objective halitosis-related measurements.

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Oral Diseases (2005) 11 (Suppl. 1), 80–82

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ORIGINAL ARTICLE

The analysis of characteristics of elderly people with high VSC level

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OBJECTIVE: The purpose of this study was to examine the characteristics of elderly subjects who had objectionable levels of volatile sulfur compound (VSC).
SUBJECTS AND METHOD: In 2002, a total of 115 85-year-old persons in Japan were subjected to oral examinations, tongue coat collections, measurements of VSCs levels inside the mouth using a portable gas chromatography (Oral Chroma™, Abilit, Japan), and assessments of quality of life (QOL) using an SF-36 questionnaire.
RESULTS: Sixty-six of the subjects were edentulous and 49 were dentulous. They were divided into two groups by VSC levels, those with oral malodor (both H_2S > 112 ppb and CH_3SH > 26 ppb; subjects with oral malodor, OM group; n = 7) and those without (n = 108). Our results showed that tongue coat deposit amounts and proportion of dentulous subjects were significantly higher in the OM group. Further, in an analysis of QOL, the SF-36 scores for vitality, social functioning and mental health were significantly higher in OM.
CONCLUSION: We found that elderly subjects with oral malodor tended to be dentulous and had large deposits of tongue coating. However, oral malodor in the OM group subjects did not appear to cause a disadvantage in their social lives.
Oral Diseases (2005) 11 (Suppl. 1), 80–82

Keywords: volatile sulfur compound; oral malodor; elderly; quality of life; SF-36

Introduction

Elderly people generally perceive that oral health is very important to their quality of life (QOL) in a variety of settings, such as eating and communication (McGrath and Bedi, 1999), and typically consider that it will be hindered by the existence of oral malodor. Many studies that have been undertaken regarding oral malodor have used a biomedical or clinical approach, with relationships with periodontal disease (Bosy *et al*, 1994), and with the degree of tongue coating and volatile sulfur compounds (VSCs) values (Miyazaki *et al*, 1995) reported. However, there are few known reports regarding the relationship between oral malodor and QOL that have used a scientific behavioral approach.

In the present study, we tested elderly subjects at 85 years of age. Recently, the so-called 80–20 movement has been promoted in Japan, which advocates that a healthy situation for the whole body exists when a person has a majority of original teeth and aims to have 20 teeth or more remaining when a person is 80 years old. Dental checkups on a nationwide scale were performed for people who were 80 years old in 1997 to prove this speculation and a database was constructed based on the results. We checked the health condition 5 years later of some of the subjects in the 80–20 database.

Subjects and methods

In 2002, a total of 115 elderly people in Japan, each 85 years old and in general good health, were examined, during which we carried out oral examinations including tongue coat deposit collection, measurements of VSC levels inside the mouth using a portable gas chromatography (Oral Chroma™, Abilit, Japan), and assessments of QOL. From the results, we attempted to determine whether oral malodor in healthy elderly people was related to one of the tested factors or to their QOL. A single examiner evaluated the subjects' tongue coat status and the score from 0 to 3 was given according to the distribution area (Miyazaki *et al*, 1995). Tongue coat samples were collected by scraping the dorsum surface with a sterile tooth brush and suspending the material in PBS. After sonication, the optical density of the suspension was determined at a wavelength of 500 nm. For detailed QOL assessments, we employed the SF-36, Japanese edition version 1.2 (Fukuhara *et al*, 1998a,b), which is a questionnaire used to present general health status as an index for evaluation of QOL. In the SF-36, one item is designed to assess any perceived change in health status and the remaining 36 items are divided into the following eight sections; physical functioning (PF), role-physical (RP), body pain, general health, vitality (VT), social functioning

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(SF), role-emotional, and mental health (MH). Data were analyzed statistically and all statistical analysis procedures were conducted using SPSS 11.5J (SPSS Inc. Chicago, IL, USA).

Results

The average number of teeth present was 4.30 ± 7.11 in all of the subjects, of whom 66 were edentulous and 49 dentate. We divided the subjects into two groups by VSC levels, those with oral malodor (both H_2S > 112 ppb and CH_3SH > 26 ppb, OM group; $n = 7$) and those without oral malodor (normal group, $n = 108$).

Based on the results of a chi-square test, the proportion of dentulous subjects in the OM group was significantly higher than in the normal group, as shown in Table 1. Further, it was shown that the amounts of tongue coat deposits were significantly higher in the OM group (Mann–Whitney's *U*-test) (Figure 1), although there was no significant difference between edentulous and dentulous subjects.

Table 1 Relationship between oral malodor and presence of teeth

	Oral malodor		
Subjects	*OM*	*Normal*	*Total*
Dentulous	6	43	49
Edentulous	1	65	66
Total	7	108	115

Values shown represent the number of subjects. Analysis was carried out using a chi-square test, $\chi^2 = 5.664$, $P = 0.041$.
OM, subjects with oral malodor (both H_2S > 112 ppb and CH_3SH > 26 ppb); normal, subjects without oral malodor.

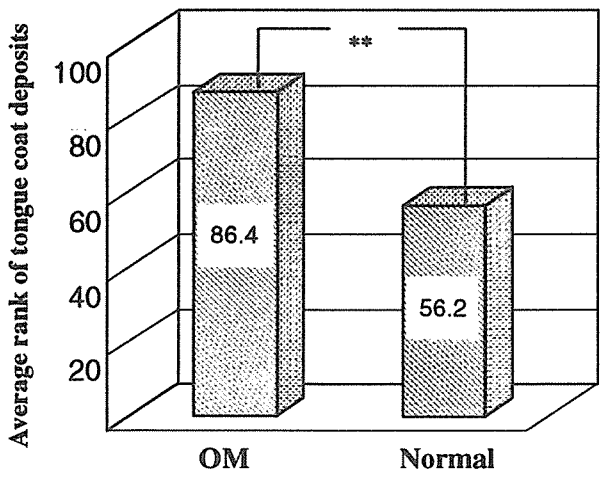

Figure 1 Relationship between tongue coat deposits and oral malodor. Mann–Whitney's *U*-test: $^{**}P < 0.01$. OM, subjects with oral malodor (both H_2S > 112 ppb and CH_3SH > 26 ppb); normal, subjects without oral malodor

Table 2 Factors related to H_2S concentration

	Tongue coat score	*Tongue coat deposit*
H_2S	0.257[a]	0.278[a]

[a]Analysis was carried out using Spearman's correlation coefficient by ranks, $P < 0.01$.

Table 3 SF-36 factors related to CH_3SH concentration

	PF	*RP*	*MH*
CH_3SH	0.187*	0.204*	0.342**

Analysis was carried out using Spearman's correlation coefficient by ranks: $^{*}P < 0.05$; $^{**}P < 0.01$.
PF, physical functioning; RP, roll-physical; MH, mental health.

To examine whether there was a difference in QOL between the OM and normal groups, we analyzed the SF-36 results using a *t*-test and found that scores for the PF, VT, SF, and MH sections were significantly higher in the OM group, which showed that the subjects with oral malodor had a tendency to have high scores for QOL, both physically and mentally. Further, we analyzed which factors were related to the levels of VSC in mouth air, especially the concentrations of H_2S and CH_3SH, and found that the concentration of H_2S was related to tongue coat score and the amount of tongue coat deposit (Spearman's correlation coefficient by ranks) (Table 2). In contrast, CH_3SH was not associated with the amount of tongue coat deposit; however, there were significant relationships to the SF-36 categories of PF, RP, and MH (Table 3).

Discussion

In Japan, more than 50% of dental outpatients are concerned about oral malodor that is actually below the sense of smell threshold and believe that their bad breath, although unable to be detected by others, hinders them from successful interpersonal relationships. In our previous study, we found that healthy high school students who were excessively concerned about bad breath below the sense of smell threshold tended to believe that their interpersonal relationships were not good (Aizawa *et al*, 2003). In contrast, the elderly subjects with oral malodor in the present study did not perceive that their social functioning or mental health were hindered. Further, the concentrations of H_2S and CH_3SH in the mouth air of the present dentulous subjects were higher than in the edentulous subjects.

It is known that the physical functions of elderly people with fewer teeth are higher than dentulous elderly subjects. However, in the present study, the QOL scores of elderly subjects with oral malodor were high both physically and mentally, regardless of the presence of teeth. These results suggest that healthy elderly people who maintained their health condition to the point of being able to come to a health checkup at the age of

85 years old, did not find that bad breath had hindered their social life. We concluded that people who are unable to manage their interpersonal relationships because of oral malodor generally are not healthy at the age of 85 years old.

Based on our findings, we speculate that measurable oral malodor does not cause a hindrance of social and interpersonal relationships, but rather the belief that bad breath exists, which may result in a decrease of QOL. In conclusion, we found that elderly subjects with oral malodor tended to be dentulous and had high levels of tongue coat deposits; however, their social life was not hindered as a result.

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Oral Diseases (2005) 11 (Suppl. 1), 89–91

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ORIGINAL ARTICLE

Relationship between the SF-36 questionnaire and patient's satisfaction following halitosis therapy

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OBJECTIVE: To assess the health-related quality of life (HRQOL) of patients complaining of halitosis at their first visit and at a later time when their complaint had diminished following therapy, using a self-administered questionnaire, the Medical Outcome Study Short Form-36 (SF-36). The aim of this study was to examine the relationship between HRQOL of patients before and after self-reported disappearance of their complaint following oral hygiene improvements for halitosis.

SUBJECTS AND METHODS: Seventy patients of our special clinic for halitosis served as subjects. At the first visit, each completed the SF-36 before determination of volatile sulfur compound (VSC) concentration in mouth air. After excluding dropouts, the same measurements were performed for subjects whose self-reported complaint had disappeared following oral hygiene therapy.

RESULTS AND DISCUSSION: At the initial visit, SF-36 scale scores for general health, vitality, social functioning, role-emotion, and mental health were significantly lower when compared with the national averages in Japan. For subjects with self-reported disappearance of complaint, only social functioning rose significantly among SF-36 scores at the end of the study. These results suggest that an awareness of improvement in social life could be related to patient's satisfaction with halitosis oral hygiene therapy.

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Keywords: outcome study; Medical Outcome Study Short Form-36; health-related quality of life; halitosis therapy

Introduction

Recently, the patient-oriented outcome of medical intervention has been studied using techniques to evaluate health-related quality of life (HRQOL) with a high degree of reliability. The Medical Outcome Study Short Form-36 (SF-36) health survey is a representative tool for determining HRQOL (Fukuhara *et al*, 1998a) and is widely used in a variety of medical fields. The disappearance of self-reported complaint in halitosis patients is considered to closely depend on HRQOL, however, its determination is not commonly used in halitosis studies. The aim of the present study was to assess the HRQOL of patients complaining of halitosis at the first visit and at the time when their self-reported complaint had disappeared following oral hygiene treatment.

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Subjects and methods

Subjects and therapy

The subjects were 70 patients (20 males, 50 females, mean age 46.7 ± 14.8 years old) who visited the Special Clinic for Halitosis at the Dental Hospital of Iwate Medical University School of Dentistry, Morioka, Japan. None had severe systemic disease and the therapy was not unusual. Briefly, it consisted of instruction regarding oral self-care, professional oral cleaning, and consultations about halitosis including explanation of the examination data, education about halitosis and reassurance. Treatments for periodontal or the other oral diseases were performed if necessary. The SF-36 questionnaire was given and measurement of volatile sulfur compound (VSC) was carried out at the first visit for all subjects, and then for those who no longer complained about halitosis following our therapy.

Definition for disappearance of complaint

For the present study, we defined a patient with disappearance of complaint about halitosis as follows. The patient received treatment three or more times over a 1-month period and, after finishing the therapy, was satisfied that their previous oral malodor was no longer a matter of concern to themselves or others. Further, they agreed to receive regular general dental check-ups after the initial therapeutic period.

Measurement of VSC in mouth air

The VSC levels in mouth air were measured using a Halimeter (Model RH-17K, Interscan Corp., Chatsworth, CA, USA) under the same conditions as reported in our previous study (Kishi *et al*, 2002).

SF-36 questionnaire and statistical analysis

The HRQOL status of each subject was evaluated using the SF-36 version 1.2, Japanese edition (Fukuhara and Suzukamo, 2001), which presents questions related to health status in eight scales: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotion, and mental health, the answers to which were analyzed using an original algorithm. All procedures concerning the questionnaire were performed according to the manual provided with the SF-36.

For statistical analysis, each of the SF-36 scores was standardized to a norm-based score and shown as a deviation value (mean: 50 ± 10) when compared with the general population in Japan (Fukuhara *et al*, 1998b). VSC concentration results were transferred to logarithms (logVSC) to obtain a near normal distribution. All statistical analysis procedures were conducted using SPSS 11.5J (SPSS Inc., Chicago, IL, USA).

Results

The average Halimeter measurement of all subjects at the first visit was 291.5 ± 417.5, while 64.1% of the subjects had a concentration <200 p.p.b. H_2S equivalent (concentration for the threshold of malodor Tonzetich, 1976). SF-36 scores for the scales of general health, vitality, social functioning, role-emotion, and mental health were significantly lower than the national averages (Figure 1). Table 1 shows the correlations between each SF-36 scale score and two principal components that are commonly considered as physical and mental components (Ware *et al*, 1994). When compared with the standard scores in Japan, it was notable that the social functioning scores of the present subjects had very little relation to a physical component.

During the present study, 17 of the subjects met our definition for disappearance of complaint for halitosis. For them, SF-36 scales and clinical parameters were compared between the first visit and at the end of the study (Figure 2, Table 2). Parameters relating to oral hygiene were significantly improved and mean VSC levels reduced following therapy although the change was not statistically significant. In the SF-36 scores, only the social functioning score rose significantly.

Subsequently, to examine whether the SF-36 is helpful to estimate the prognosis of halitosis patients, we performed a multiple logistic regression analysis, in which SF-36 scale scores for all the subjects were used as independent variables. In addition, the patient residence location information was added to the regression analysis, as the time required commuting between home and clinic might have been a considerable factor for those who dropped out of the study. At the conclusion of the regression analysis, only social functioning and mental health scores were shown to be significant variables, with odds ratios of 0.948 and 1.077, respectively (Table 3).

Table 1 Associations between SF-36 scales and rotated components

	Japanese standard[b]		*Present subjects*	
	Physical[a]	*Mental*[a]	*Physical*[a]	*Mental*[a]
Physical functioning	0.75	0.17	0.75	0.02
Role-physical	0.81	0.19	0.66	0.42
Bodily pain	0.51	0.52	0.62	0.03
General health	0.37	0.66	0.36	0.02
Vitality	0.21	0.88	0.16	0.81
Social functioning	0.45	0.60	0.03	0.70
Role-emotion	0.69	0.34	0.50	0.64
Mental health	0.13	0.89	0.04	0.88

Correlations are shown between each Medical Outcome Study Short Form-36 (SF-36) scale and the principal component.
[a]Two principal (physical and mental) components were extracted from the SF-36 scores of all subjects and rotated to an orthogonal simple structure using a varimax method.
[b]Data from a previous study (Fukuhara *et al*, 1998a).

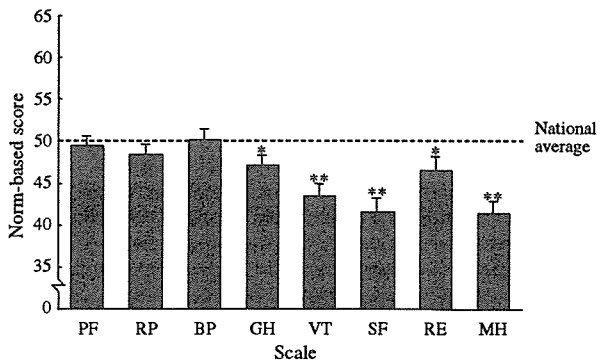

Figure 1 Average Medical Outcome Study Short Form-36 (SF-36) scores for all patients at the first visit. Norm-based score shows mean ± s.d. for the general population in Japan, which is 50 ± 10. The vertical bar (T) shows the s.e. Analysis of each sample was done with a *t*-test by comparing with the national average, $*P < 0.05$ and $**P < 0.01$. PF, physical functioning; RP, role of physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role of emotion; MH, mental health

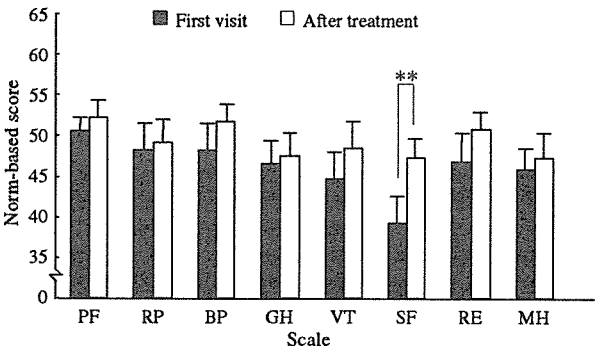

Figure 2 Medical Outcome Study Short Form-36 (SF-36) scores in subjects with disappearance of complaint. Average SF-36 scores at the first visit and following treatment for 17 patients with disappearance of complaint were compared. The vertical bar (T) shows the s.e. **Analysis was done using a paired t-test, $P < 0.01$. PF, physical functioning; RP, role of physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role of emotion; MH, mental health

Table 2 Clinical parameters before and after the treatment

	First visit	*After treatment*
VSC (p.p.b.)[a]	347.8 ± 91.7	210.8 ± 36.4
logVSC	2.33 ± 0.11	2.23 ± 0.07
Tongue score[b]	1.47 ± 0.24	0.94 ± 0.20**
Pocket depth (mm)[c]	3.33 ± 0.19	3.00 ± 0.22*
Bleeding tooth rate (%)[d]	41.5 ± 5.27	25.2 ± 5.27*
PCR (%)[e]	43.6 ± 5.05	27.1 ± 2.69*

Values represent mean ± s.e.
[a]VSC concentration in mouth air determined by Halimeter.
[b]Tongue coat score obtained by inspection according to a previous study (Miyazaki *et al*, 1995).
[c]Maximum pocket depth among recorded six sites of all measurable teeth.
[d]The rate tooth showing bleeding on probing among all measurable teeth.
[e]Percentage index of Plaque Control Record (Podshadley and Haley, 1968).
Comparison between the averages before and after treatment by paired *t*-test: $*P < 0.05$, $**P < 0.01$.
VSC, volatile sulfur compound; PCR, polymerase chain reaction.

Table 3 Significant variables for prediction whether the complaint could disappear or not

Variable	*B*	*s.e.*	*P*-value	*Exp(B)*	*95% CI*
Social functioning	−0.54	0.24	0.025	0.948	0.904–0.993
Mental health	0.75	0.34	0.029	1.077	1.008–1.152

The dependent variable was disappearance of complaint (disappearance: 1, others: 0). Independent variables were each SF-36 scale score and the subject residence location (same city as our clinic: 1, neighboring city/town: 2, distant city/town with good traffic condition: 3, distant city/town with poor traffic condition: 4, another prefecture: 5). B, partial regression coefficient; CI, confidence interval; Exp(B), exponent of partial regression coefficient (=odds ratio); SF-36, Medical Outcome Study Short Form-36.

Discussion

At the first visit, SF-36 scores for the 70 subjects in the scales of general health, vitality, social functioning, role-emotion, and mental health significantly differed from those of the national standard. Among them, social functioning seemed to best represent the characteristics of the halitosis patients that visited our special clinic. Based on a principal component analysis, social functioning was strongly related to the mental component, however, not the physical component. We considered that this represented a failure in social functioning that was closely associated with the mental health of our patients. These results suggest that, at least for the present subjects, halitosis complaints may be derived mainly from a decline of social functioning.

Among the patients whose complaint was eliminated, average VSC did not show a significant reduction following our treatment. The high standard error of mean VSC values reflects the wide range of VSC levels found in the population at large. This wide scatter may hide the differences obtained through treatment. It is obvious that a reduction of VSC level is the main goal of halitosis therapy; however, in patients whose VSC level is comparatively low at the start of treatment, the outcome of clinical intervention will not be clearly demonstrated. Whilst an improvement in halitosis (as measured by lowering of VSC levels) could not be shown statistically, patients may still show satisfaction following the therapy, as in the present subjects. Our present study suggested that the disappearance of complaint of halitosis in subjects can be related to an improvement in social functioning score following improvement of their oral hygiene.

We tried to develop a prognosis model for halitosis patients by using the SF-36. By means of a stepwise procedure of logistic regression analysis, social functioning and mental health were shown to be significant variables. Furthermore, there was a tendency for patients with low social functioning and high mental health scores to have a high possibility that the initial complaint could disappear by our ordinary remedy for halitosis, although the odds ratios were too small to obtain a sufficient estimation for prognosis.

In conclusion, patient's satisfaction following halitosis therapy relates to HRQOL of the patients, especially to social functioning.

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レクチャー

口臭診療の実際

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（受付：17年11月7日）
（受理：17年11月7日）

Key words：Halitosis, Volatile sulfur compounds, Illness, Explanatory model, QOL

1．はじめに

口臭は，臭気物質の主たる成分が歯周病原性細菌の代謝産物の揮発性硫化物質である[1,2]ことから，主に歯周病患者を対象として，その症状との関連あるいは歯周病のリスクインディケータとしての有用性が研究されてきた[3-8]。しかし口臭は歯周病のない者にも存在し，全身状態との関連も示唆されている[9]ことなどから，一般に口臭を口腔保健のなかで重視する傾向が高まっている。我が国においても近年，国民が自覚する口腔の問題点として上位に位置するようになった（図1）。このような背景から，大学附属病院などで口臭に関する専門外来が開設され，また一般の歯科診療所でも口臭を主訴とする患者を受け入れるようになってきた。しかし，口臭患者に対する標準的治療法は確立されていないのが現状である。そこで本稿では，歯科診療所における口臭診療への取組みの参考として，口臭に関する一般的知見とともに，岩手医科大学附属病院歯科医療センター口臭外来で行われている口臭診療の内容を紹介する。

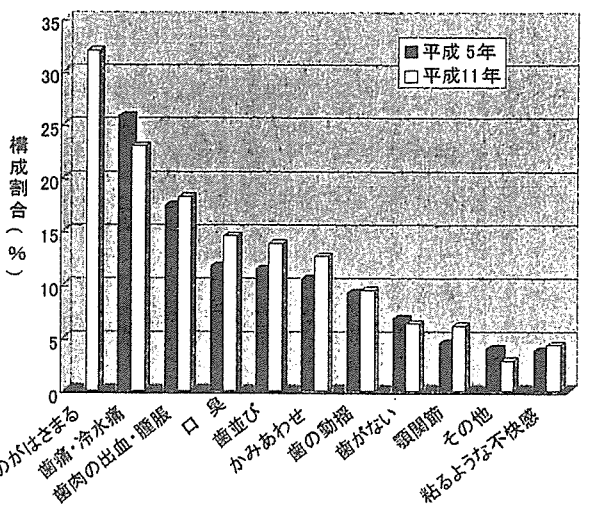

図1：日本人の歯や口に関する悩み（厚生労働省保健福祉動向調査）

Introduction of practical therapy for halitosis.
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表1：官能検査の判定基準[10]

スコア	判定基準
0：臭いなし	臭覚閾値以上の臭いを感知しない。
1：非常に軽度	臭覚閾値以上の臭いを感知するが，悪臭と認識できない。
2：軽度	かろうじて悪臭と認識できる。
3：中等度	悪臭と容易に判定できる。
4：強度	我慢できない強い悪臭。
5：非常に強い	我慢できない強烈な悪臭。

2．口臭の測定法と臭気物質

多くの場合，口臭を訴える患者の診断，治療のためには口臭を測定することが必要である。口臭を測定する方法は2種類に大別される。ひとつは官能試験であり，もうひとつは機器による測定法である。

1）官能試験

検査者が，実際に患者の呼気の臭いを嗅いで判定する方法である。官能試験の正確な実施は以下のように行う。

検査者と患者はお互いの姿が見えぬよう，パネルをはさんで向かい合う。これは患者のプライバシー保護と同時に，検査する者が，外見などにより先入観を抱かないようにするためである。患者はパネル中央に通したチューブに呼気を吐き出し，検査者がその臭いを評価基準に従って判定する（図2）。検査者には標準ガスで臭いを評価するための訓練をした3人以上の者があたり，その最頻値をスコアとする。官能試験の代表的な判定基準を表1に示した。また，測定は雑音の少ない個室で行う。これは口臭以外の臭気の遮断と測定者が判定に集中できる環境を作るためである。

以上のように，厳密に行えば，官能試験の信頼性は高いものとなる。しかし日常的にそのような方法をとることは，多くのスタッフが存在する大学附属病院においても困難である。それ故，当口臭外来では，簡便な方法として，担当医が患者から一定の距離（40cm）をおいて呼気の臭いを判定している。その際，担当医は匂いの強い石鹸の使用，コーヒー摂取，喫煙といった，判定の障害になる行為は避けることとして

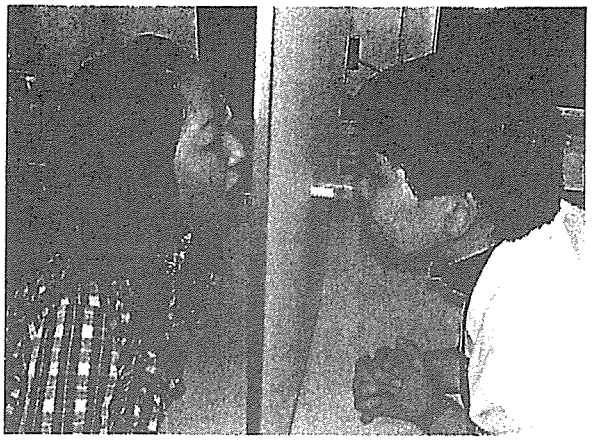

図2：口臭測定のための官能試験

いる。官能試験は検査者の主観的判定であるため，特に簡便法では再現性や定量性に問題がある。しかし，後述する機器による測定に対していくつかの利点がある。まず，機器測定では，特定の揮発性ガスだけを測定しているのに対し，官能試験は機器では測定不可能な，あらゆる臭気物質が混合された状態を評価していることである。また，口臭が第三者に知覚される状態を判定しているため，日常生活で問題となる口臭に近い状態を再現していると考えられる。患者のなかには機器による測定結果に不信感を抱く者が少なくない。そのような者に対して正確な方法で官能試験を行うと，少なくとも機器測定結果以上には判定結果を信用してもらえる例は多い。

2）機器による測定法

口中気体のある特定の臭気物質の濃度を，測定機器を用いて定量的に測定する方法である。ここで呼気ではなく，口中気体と表現するのは，これら機器のほとんどが，口から吐き出した呼気ではなく，一定時間閉口後に採取した口

表 2 ：呼気中の臭気物質

窒素化合物	アンモニアなど揮発性アミン類，インドール，スカトール
脂肪酸	酢酸，イソ酢酸，プロピオン酸など
アルデヒド	アセトアルデヒド
ケトン	アセトン
硫黄化合物	硫化水素，メチルメルカプタン，ジメチルサルファイド

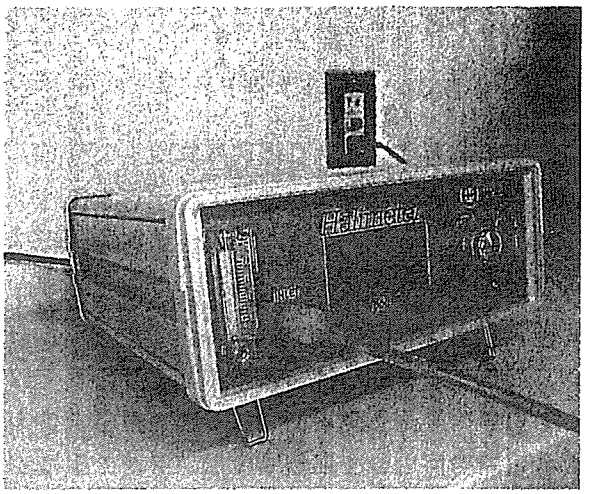

図 3 ：ポータブルサルファイドモニター（ハリメーター®）

腔内の気体を測定に供するためである。臭気物質には，窒素化合物，揮発性脂肪酸，アセトアルデヒド，アセトン，硫黄化合物（Volatile Sulfur Compounds ; VSC）などがある（表 2）。このうち VSC は他の臭気物質よりもはるかに低濃度でヒト嗅覚閾値に達することから，ヒトが感知する口臭の最も大きな原因物質と考えられている。実際に，硫化水素の嗅覚閾値が100ppb 程度なのに対して，酢酸は 1 ppm，アセトンは100ppm という高濃度であり，口臭程度の評価には VSC 濃度を測定することが一般に用いられている。VSC を測定する機器にはいくつかあるが，世界的にもっとも広く用いられているのは，米国インタースキャン社のハリメーター®である（図 3）。これはポータブルサルファイドモニター[11]とよばれる VSC の総量を測定する機器である。デジタル表示により VSC 濃度が ppb 単位で表示される。この装置を用いた測定の通法は以下の通りである。

患者に 2 分間閉口，鼻呼吸してもらった後，息を止めた状態で測定器の吸引ストローをくわ

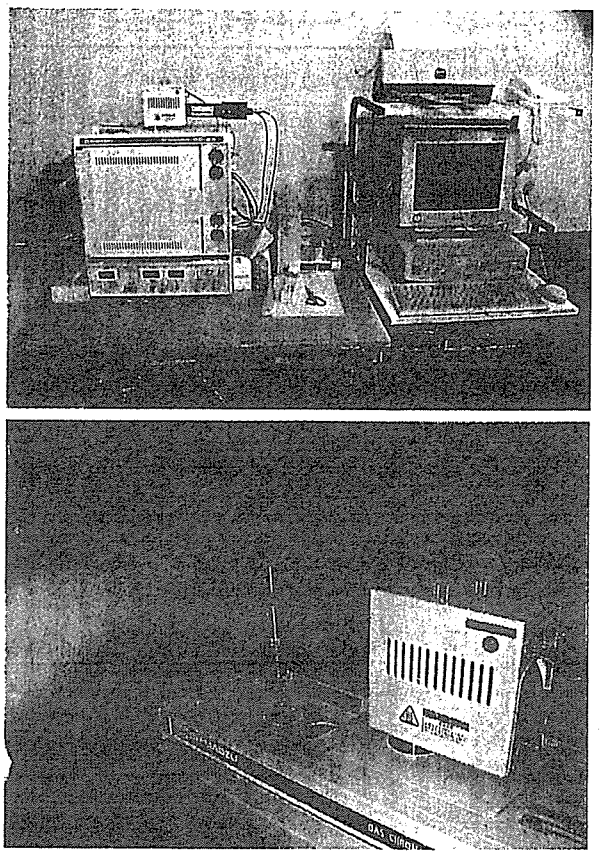

図 4 ：ガスクロマトグラフィ
上段：ガスクロマトグラフィの測定システム。本体は左側の機器。測定結果は右側のパーソナルコンピュータのモニターに表示される。また，これ以外にキャリアガスと水素ガスのボンベ，コンプレッサー，キャリブレーションのための標準ガス発生装置を必要とする。
下段：ガスクロマトグラフィに採取した口中気体を注入しているところ。

えてもらう。この際，口唇は軽く開いた状態とする。その状態を10秒間保持し，デジタル表示の最大値を読み取る。正確に測定するためには，測定前に患者に練習してもらうなどの準備が必要である。

VSC 測定のための機器として，現在ゴールドスタンダードとされているのはガスクロマトグラフィ[1]である。当口臭外来では島津 GC-8

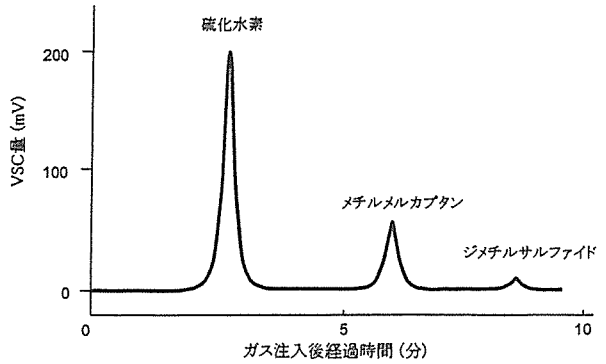

図5：ガスクロマトグラフィによるVSC検出パターン
ガスクロマトグラフィによるVSC検出パターンの一般的な例。検出ピークは硫化水素，メチルメルカプタン，ジメチルサルファイドの順である。それぞれのピーク高さから，分析ソフトにより各気体の濃度が算出される。

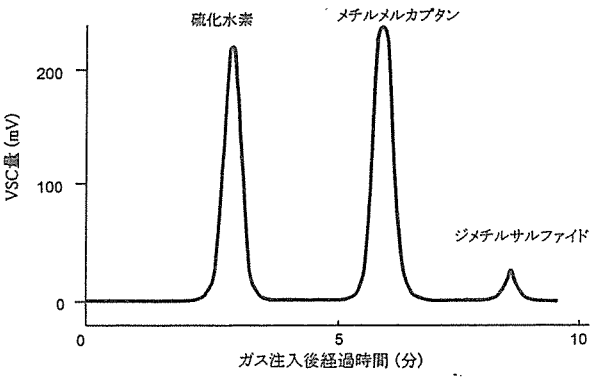

図6：歯周炎患者の口中気体からのVSC検出パターン

という機種を導入している（図4）。この検査では2分間閉口した状態の口中気体を自動的あるいはガスタイトシリンジを用いて採取し，注入する。ガスクロマトグラフィのハリメーター®に対する優位性は，測定の正確さだけでなく，3種類のVSCすなわち硫化水素，メチルメルカプタン，ジメチルサルファイドを弁別定量できる点にある。また，臭気物質の検出が波形のピークで表示されるため，患者に対するプレゼンテーション効果も高いと考えられる（図5）。ガスクロマトグラフィの欠点は，装置自体と維持費が高価であること，機器設置面積が大きいこと，システムを起動してから測定可能な状態に安定するまで，30～60分必要なこと，測定に15分程度時間を要することが挙げられる。すなわち日常診療の中で応用するには機器の規模が大きいことが欠点である。実際我々はこの機器のために診療室とは別に測定室（兼，相談室）を設けている。最近，安価でポータブルのガスクロマトグラフィが開発され(Oral Chroma®, ABILIT，大阪)，一部の歯科診療所でも導入されている。しかしシステム起動から安定までの時間と測定に要する時間は従来のガスクロマトグラフィとそれほど変わらず，その点での改良が望まれる。

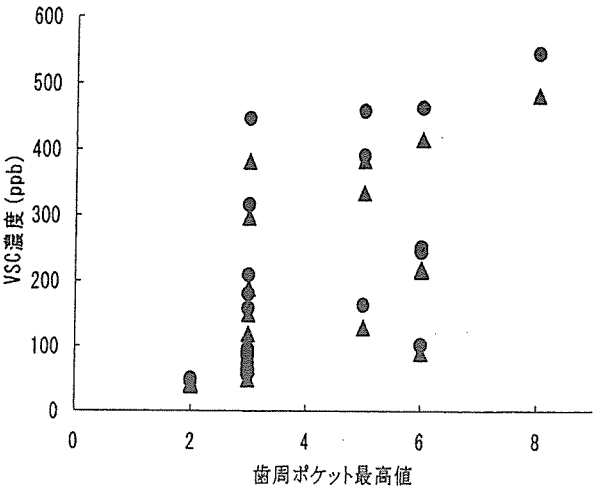

図7：口臭外来受診者（N＝40名；男性14名，女性●26名）の口中気体VSC濃度（ハリメータ®により測定）と歯周ポケット最大値の関連。順位相関係数0.692（$p<0.01$）と高い相関が認められた。

3．口臭の種類と原因

口臭には口腔由来と全身疾患を原因とするものとがある。しかし全身疾患に起因する口臭については研究事例が少なく，臨床的にも稀であることから[9,12]，日常的に診療対象とする口臭のほとんどは口腔由来と考えられる。口腔由来の口臭はさらに生理的口臭と歯周病由来の口臭に区別できる。ガスクロマトグラフィで口臭を測定すると，生理的口臭の場合は，図5のようにVSCのうち主として硫化水素が検出される。これに対して深い歯周ポケットを形成している歯周炎患者の口臭からは硫化水素と同等かそれ以上のピークとしてメチルメルカプタンが検出される（図6）。

生理的口臭は起床時，空腹時など口腔の活動が長時間休止している場合に強くなる。また，舌苔の付着量が多い場合にも生理的口臭は強くなる[13-15]。

歯周病由来の口臭は生理的口臭と同様の日内変動を呈するが，その程度は歯周病の重症度，活動性などに強く依存している（図7）。

4．口臭を訴える患者への対応

前項で，口臭を分類したが，臨床上よく用いられるもう一つの分類に，いわゆる他臭症と自臭症というものがある。すなわち，口臭を訴える者のうち，他覚的な口臭がない者を自臭症と称し，心因性の要素が強い患者として他覚的な口臭を有する患者と区別するものである。このような患者の訴えと，口臭測定結果の差違は，これまで多くの臨床家を悩ませ，自臭症患者の特性や対応についてさまざまな検討がなされてきた[16-20]。さらに最近ではその矛盾を解消するために，機器による臭気物質の検出感度の向上[21]や自臭症患者を仮性口臭症と口臭恐怖症に細分類し，口臭恐怖症については精神医学専門家へ依頼することで対応する[10,22]，などの方法論が検討されている。一方，近年，メディカルインタビューの概念が浸透し，患者のなかにある病（illness）と医療者の診断（disease）の差違を認識することが，医療者にとって重要であると考えられるようになった[23]。「自臭症」，「口臭恐怖症」という分類はdiseaseである。これに対してillnessとはすなわち患者の主観的部分である。同じような症状を訴えても，受診に至る背景は個々に異なっており，病気に関する解釈もまたさまざまである。Kleinmanは症状に対する患者の意味づけを〝解釈モデル〟と呼び，それを理解することの臨床的意義を指摘した[24]。このような考え方を背景として，我々は，口臭を訴える者を，他覚臭の有無で分類するのでなく，その患者固有の口臭に対する解釈モデルを理解するよう努めることで，さまざまな口臭に関する訴えに対応することを選択してきた。

口臭患者の解釈モデルは一様ではないが，これまでの我々の臨床経験からいくつかの類型があると考えられる。代表的なものを挙げると，

1）自分ではさほど気にならないが，妻など近親者に指摘されて受診した場合。患者は指摘した近親者を信頼しており，その指示に従って受診することが主たる目的である。受診することで目的の大半は達成されており，口臭をそれほど重要な問題とは認識していない。

2）口臭をより重篤な疾患の前兆ではないかと危惧している場合。口臭それ自体より，想像される全身疾患などに対して強い不安を感じている。口臭の検査を通じて重篤な疾患を発見してもらいたいと希望している。

3）口臭によって人間関係など社会的側面で悪い影響が及ぼされていると感じている場合。口臭さえなければ自分はもっと思い通りの生き方ができると考えている。

などである。

これらの類型は口臭強度とある程度の関連があり，口臭が強い者では1）や2）が多く，3）の類型はいわゆる自臭症で現れやすい傾向にある。しかし口臭が強い者で3）の類型を呈することも稀ではなく，一概に他覚的口臭の強度からだけでは区別できない。また，患者は「口臭」という症状に固執しているため，初診時に明確な解釈モデルを得ることは困難な場合も多い。解釈モデルを理解することは，患者との十分な対話からのみ可能である。

専門家によるクライアントに対する対話を用いた援助方法には「ガイダンス」，「コンサルテーション」，「カウンセリング」の3種類がある[25]。ガイダンスは知識や情報の伝達である。コンサルテーションは個別の問題に対する解決方法の提示である。カウンセリングは一般的な保健指導の場合では知識や情報があり，方法も身に付いているのに実行できない場合などに，行動変容や気づきのための支援を行うことである。口臭を訴える患者に関しては，口臭への不安や拘泥がとれない場合に行う。これらの援助方法は，解釈モデルの上記類型に必ずしも対応