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ORIGINAL ARTICLE

Modeling mucosal dimensions after implantation of a bio-absorbable membrane for surgical root coverage

Hans-Peter Müller

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Abstract The aim of this study was to model alterations of mucosal thickness after implantation of a bio-absorbable membrane for surgical root coverage employing guided tissue regeneration. Periodontal conditions around 31 recession sites in 14 patients were assessed for up to 12 months after surgery. Mucosal thickness was modeled in a multivariate, three-level (occasion, tooth, subject) time series model. The amount of root coverage was studied in a bivariate multilevel model of change and mean recession to avoid mathematic coupling. Predictions of gingival thickness were, at the outset, strongly related to baseline gingival width. At maxillary teeth, gingival thickness at all measurement locations peaked 3months after surgery with negative relations to baseline gingival width. Thereafter, thickness gradually decreased but remained higher (0.3–0.5mm, 95% confidence interval 0.05–0.9mm) than before surgery, while positive correlations with baseline gingival width were re-established. At mandibular teeth, gingival thickness did not change so dramatically, while thickness of lining mucosa underwent similar changes as at maxillary teeth. In contrast to previous publications, modeling change of recession depth and mean recession did not yield better results in deeper sites when applying a bivariate multilevel model that avoids mathematic coupling.

Keywords Surgical root coverage · Bio-absorbable membrane · Gingival dimensions · Multilevel modeling · Mathematic coupling

H.-P. Müller (✉)
Institute of Clinical Dentistry (IKO), Faculty of Medicine,
Tromsø University,
9037 Breivika, Norway
e-mail: hans-peter.muller@fagmed.uit.no

Introduction

Guided tissue regeneration may be a treatment option for surgical correction of gingival recession. According to a recent systematic review of the literature, treatment outcomes may range from modest to excellent [1]. However, predictability seems to be less when compared to connective tissue-grafting techniques [18]. Apart from achievable root coverage, the implantation of a membrane and concomitant coronal advancement of the flap leads to an immediate increase in thickness of gingiva [15] and later in width of keratinized tissue [1] and, of course, considerable displacement of the mucogingival border. Hence, the entire gingival unit will undergo dramatic changes.

Covariates describing the clinical appearance of the soft tissues of the periodontium, their alterations after surgical intervention, and respective interactions may ideally be modeled in multivariable/multivariate and, if appropriate, multilevel analyses to better predict surgical outcomes. The few available studies are often prone to problems such as multicollinearity or mathematic coupling or both [27, 25]. The aim of the present reanalysis of data collected in a longitudinal study [15] was to explore alterations of mucosal dimensions, i.e., thickness and width, after surgical root coverage employing a bio-absorbable membrane for up to 12 months postsurgically by using a multilevel time series model. The main question was whether gain of tissue can be traced in the follow-up data. In addition, the amount of root coverage was studied in a recently described bivariate model, which avoids mathematic coupling while allowing easy interpretation of covariates [12].

Materials and methods

The study protocol, inclusion and exclusion criteria of the studied population, clinical variables and their respective reliabilities, the surgical procedure, certain observations during the immediate postsurgical period, and more descriptive 12-month results have been reported in a previous publication [15]. In brief, 14 nonsmoking patients, ten of whom were women, presented with a large variety of recession types and were treated during 1996 through 1997. The total sample consisted of 31 recessions, 19 in the maxilla and 12 in the mandible. According to Miller's classification [11], five recessions were class III, 11 were class II, and 15 were class I. The majority of teeth were canines (48%), followed by first and second premolars (45%), and two maxillary molars. Surgical root coverage consisted, after periosteal dissection, of a coronally advanced flap secured with sling sutures. Tissue regeneration was promoted by implanting a bio-absorbable membrane (Guidor Matrix Barrier, PPS narrow or wide; Guidor AB, Huddinge, Sweden). During surgery, the bony dehiscence, i.e., the distance between the cemento-enamel junction and crest of the alveolar bone, was measured at the midbuccal prominence of the root with a periodontal probe (PUNC15, Hu Friedy, Leimen, Germany) to the next 0.5mm. The "true" dehiscence was then calculated by subtracting the amount of recession (see below) from the bony dehiscence. Pre- and postoperative assessment of the clinical condition of the buccal/facial dentogingival unit of the particular tooth included the gingival index [10], the plaque index [21], and the probing depth as measured with an automatic probe (PeriProbe, Vivacare, Schaan, Liechtenstein) to the next 0.1mm. A caliper was used to measure recession depth, i.e., the distance between the cemento-enamel junction and the gingival margin, and its width with the intersection of the cemento-enamel junction and the gingival margin as reference points to the next 0.1mm. Clinical attachment loss was calculated by adding probing and recession depths. The width of gingiva at the maximum prominence of the root was also measured with the caliper. Thickness of gingiva at the gingival margin and at the mucogingival border, as well as thickness of the lining mucosa, were determined with an ultrasound device (SDM, Austenal, Cologne, Germany) as has extensively been described in previous publications [5, 13, 17]. The precision of the measurement was 0.1mm.

Patients were followed-up for 1year, and re-examinations of the clinical situation took place after 3, 6, 9, and 12 months.

Data analysis

Data were analyzed using the multilevel software package *MLwiN* (version 2.02, Center for Multilevel Modeling, Bristol University, Bristol). Three-level (occasion, tooth, subject) time series models were built for gingival thickness, its width, and the location of the mucoginval border in relation to the cemento-enamel junction at the buccal prominence of the root [6]. Outcomes were modeled with covariate time (in months) at examination occasion, including its linear, quadratic, and cubic components. Mucosal thickness was then modeled at all three measurement locations in a multivariate time series model with time (linear, quadratic, and cubic components), gingival width, jaw, as well as respective interactions with time as covariates. Recession type according to Miller's classification did not reveal significant effects on mucosal thickness and was not considered in the final model. Predictions of mucosal thickness and respective 95% confidence intervals were calculated for various examination occasions, different gingival widths, and jaws. In another model, root coverage was modeled with the mean of recession at baseline and after 12 months as well as its respective difference as bivariate responses [12]. A "best-fit model" was sought where only significant covariates ($p < 0.1$) for either response were entered into the model.

Results

The considerable alterations of mucosal thickness at the three different locations after surgical root coverage and implantation of a bio-absorbable membrane are displayed in Fig. 1. A dramatic increase in thickness in all locations 3months after surgery was followed by a gradual decrease thereafter. Twelve months after the intervention, median thickness was somewhat greater than before surgery. As can

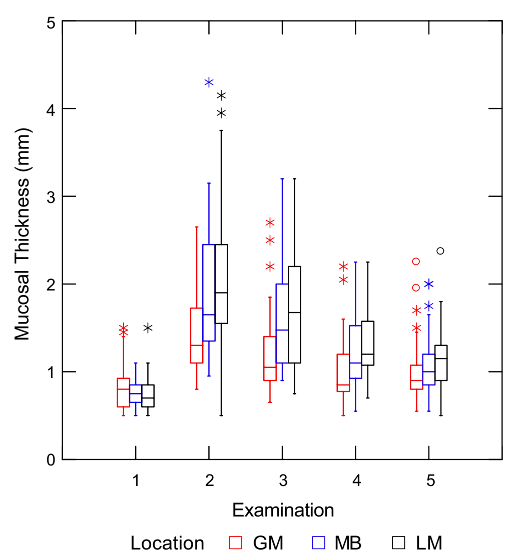

Fig. 1 Box plot representation of thickness of gingiva at the gingival margin (*GM*), the mucogingival border (*MB*), and thickness of the lining mucosa (*LM*) before (*examination 1*) and at 3-month follow-up examination intervals (*examinations 2–5*). Median, upper and lower quartiles, lowest and largest nonoutlier values, as well as mild (*asterisks*, between 1.5 and 3 times the interquartile range, IQR) and extreme outliers (*circles*, more than three times the IQR) are given

be seen in the box plot diagram, individual variation in particular at measurement points at the mucogingival border and in the lining mucosa dramatically increased as well and was still high after 12 months (Fig. 1).

Time series models of gingival thickness and width, as well as the location of the mucogingival border, are shown in Table 1. Gingival thickness increased by an estimated 0.37mm per month (95% confidence interval 0.27, 0.47mm), but deceleration was significant as well with −0.07mm per month squared (−0.05, −0.09mm). Furthermore, the cubic term was significant. Variance partition revealed that 59% of the unexplained variance of gingival thickness was still found at the occasion level and 40% at the tooth level. There was no influence of time on gingival width. Seventy-one percent of the unexplained variance of gingival width was at the occasion level as compared to 12% and 17% at tooth and subject levels, respectively. The shifts in the location of the mucogingival junction in relation to the cemento-enamel junction were significant with a linear component of −0.67mm per month (−1.05, −0.29mm) and significant quadratic and cubic components. Variance partition revealed 54% of unexplained variance still at the occasion level and 36% at the tooth level (Table 1).

The surgical intervention aimed in a change of the whole gingival unit. Modeling thickness of facial mucosa was thus done at all three measurement locations with multivariate responses in a time series model, including time, baseline gingival width, and jaw as covariates, as well as respective interactions with time (Table 2). Obviously, the highly significant linear increase in mucosal thickness with time was considerable with a mean of between 0.75 (0.57, 0.94) and 1.1mm (0.85, 1.34mm) per month, but quadratic (deceleration) and cubic terms were highly significant as well. Baseline gingival width was significantly associated with gingival thickness as measured at the gingival margin.

Table 1 Three-level (occasion, tooth subject) time series models of gingival thickness at the gingival margin (GTH), gingival width (GW), and location of the mucogingival border in relation to the cemento-enamel junction (MB) before and at follow-up after surgical intervention (exams every 3 months for up to 12 months)

Parameter	GTH	GW	MB
Fixed part			
Intercept b_{jkl}	0.838 (0.077)	1.853 (0.234)	4.641 (0.341)
t^a	0.371 (0.049)	−0.034 (0.147)	−0.670 (0.194)
t^2	−0.069 (0.010)	0.018 (0.031)	0.107 (0.041)
t^3	0.003 (0.001)	−0.001 (0.002)	−0.005 (0.002)
Random part			
Subject σ^2_{fl}	0.003 (0.016)	0.229 (0.167)	0.289 (0.395)
Tooth σ^2_{vkl}	0.070 (0.027)	0.149 (0.116)	1.088 (0.453)
Occasion σ^2_{ujkl}	0.104 (0.013)	0.948 (0.120)	1.646 (0.209)

[a] Time (in months)

Table 2 Fixed effects estimates (mm) with standard errors in brackets of a multivariate, three-level (occasion, tooth, subject) time series model of thickness of mucosa at the gingival margin (GM), at the mucogingival border (MB), and of the alveolar lining mucosa (LM) before and at follow-up after surgical intervention (exams every 3 months for up to 12 months)

Parameter	GM	MB	LM
Intercept β_{mjkl}	0.557 (0.161)	0.583 (0.203)	0.675 (0.217)
t^a	0.756 (0.094)	1.091 (0.126)	0.965 (0.161)
t^2	−0.143 (0.020)	−0.202 (0.026)	−0.169 (0.033)
t^3	0.007 (0.001)	0.010 (0.001)	0.008 (0.002)
GW[b] (mm)	0.114 (0.056)	0.063 (0.069)	0.025 (0.075)
$t\times$GW	−0.117 (0.034)	−0.154 (0.044)	−0.142 (0.056)
$t^2\times$GW	0.023 (0.007)	0.032 (0.009)	0.026 (0.012)
$t^3\times$GW	−0.001 (0.000)	−0.002 (0.000)	−0.001 (0.001)
Jaw[c]	0.215 (0.160)	0.141 (0.200)	0.086 (0.220)
$t\times$Jaw	−0.456 (0.099)	−0.430 (0.128)	0.139 (0.163)
$t^2\times$Jaw	0.087 (0.021)	0.082 (0.027)	−0.028 (0.034)
$t^3\times$Jaw	−0.004 (0.001)	−0.004 (0.001)	0.001 (0.002)

[a] Time (in months)
[b] Baseline gingival width (in mm)
[c] Mandible=1, maxilla=0

This influence decreased drastically with time after surgery, with quadratic and cubic terms being also significant. While mucosal thickness was not significantly greater at mandibular teeth in general, the interaction with time was negative and highly significant for gingival thickness, with significant quadratic and cubic components (Table 2).

The random part of the model is shown in Table 3. Variances and covariances at the subject level were not significant. At the tooth level, the significant ($p < 0.05$) covariance for thickness at different locations, say m and n, yielded very high correlation coefficients (calculated as $r_{m,n} = \sigma_{m,n}\big/\sqrt{\sigma^2_m \times \sigma^2_n}$) of between 0.8 and 0.98. Thus, even thickness of lining mucosa was highly correlated with gingival thickness at both measurement locations. At the occasion level, correlation coefficients were essentially weaker (Table 3).

Predictions of mucosal thickness as derived from the model (Table 2) are shown in Fig. 2. In general, estimated 95% confidence intervals were low, ±0.2–0.3mm at maxillary teeth and ±0.4–0.5mm at teeth in the mandible. At the outset, gingival thickness was positively correlated with gingival width. For example, at maxillary teeth, gingival thickness at the gingival margin was estimated as 0.67mm (0.43, 0.91mm) in case of 1-mm-wide gingiva, 0.78mm (0.59, 0.98mm) at 2-mm-wide gingiva, 0.90mm (0.68, 1.11mm) at 3-mm-wide gingiva, and 1.01mm (0.74, 1.28mm) at 4-mm-wide gingiva. In the maxilla, mucosal thickness at all measurement locations peaked 3months after surgery with negative correlations with baseline gingival width. Thereafter, thickness gradually decreased but remained higher (0.3–0.5mm, 95% confidence interval

Table 3 Random part of multivariate, two-level (occasion, subject) model of gingival thickness at the gingival margin (GM), the mucogingival border (MB), and of the lining mucosa (LM)

	Parameter	GM	MB	LM
Subject	$\sigma^2_{fl,m}$	0.024 (0.020)	0.026 (0.023)	
	$\sigma_{fl,m,m+1}$	0.026 (0.021)		
Tooth	$\sigma^2_{vkl,m}$	0.055 (0.022)	0.083 (0.033)	0.064 (0.029)
	$\sigma_{vkl,m,m+1}$	0.067 (0.025)	0.066 (0.025)	
	$\sigma_{vkl,m,m+2}$	0.048 (0.020)		
Occasion	$\sigma^2_{ujkl,m}$	0.089 (0.011)	0.139 (0.018)	0.223 (0.029)
	$\sigma_{ukl,m,m+1}$	0.039 (0.011)	0.041 (0.017)	
	$\sigma_{ukl,m,m+2}$	0.022 (0.013)		

Standard error in parentheses

0.05, 0.5 and 0.1, 0.9mm, respectively) than before surgery, while positive correlations with baseline gingival width were re-established (Fig. 2, left panel). At mandibular teeth, gingival thickness did not change so dramatically, while thickness of lining mucosa underwent similar changes as at maxillary teeth (Fig. 2, right panel).

A bivariate, three-level, "best-fit" model for responses (1) change after surgical root coverage, and (2) the mean of pre- and postsurgical recession is shown in Table 4. Note that the lowest level defines the multivariate structure with higher levels of tooth and subject. Both change in recession and mean recession were significantly associated with tooth type. For example, as compared to other teeth, canines responded better with, on average, 0.57 mm more root coverage (0.13, 0.98 mm). The "true" bony dehiscence as measured during surgical intervention had a negative impact on change. Only gingival thickness at the mucogingival border negatively influenced mean recession. The random part of the model revealed nonsignificant covariances between change and mean recession (Table 4). Thus, deeper sites did not yield better results in terms of root coverage. Gender and Miller class did not significantly influence root coverage and were therefore not entered into the model.

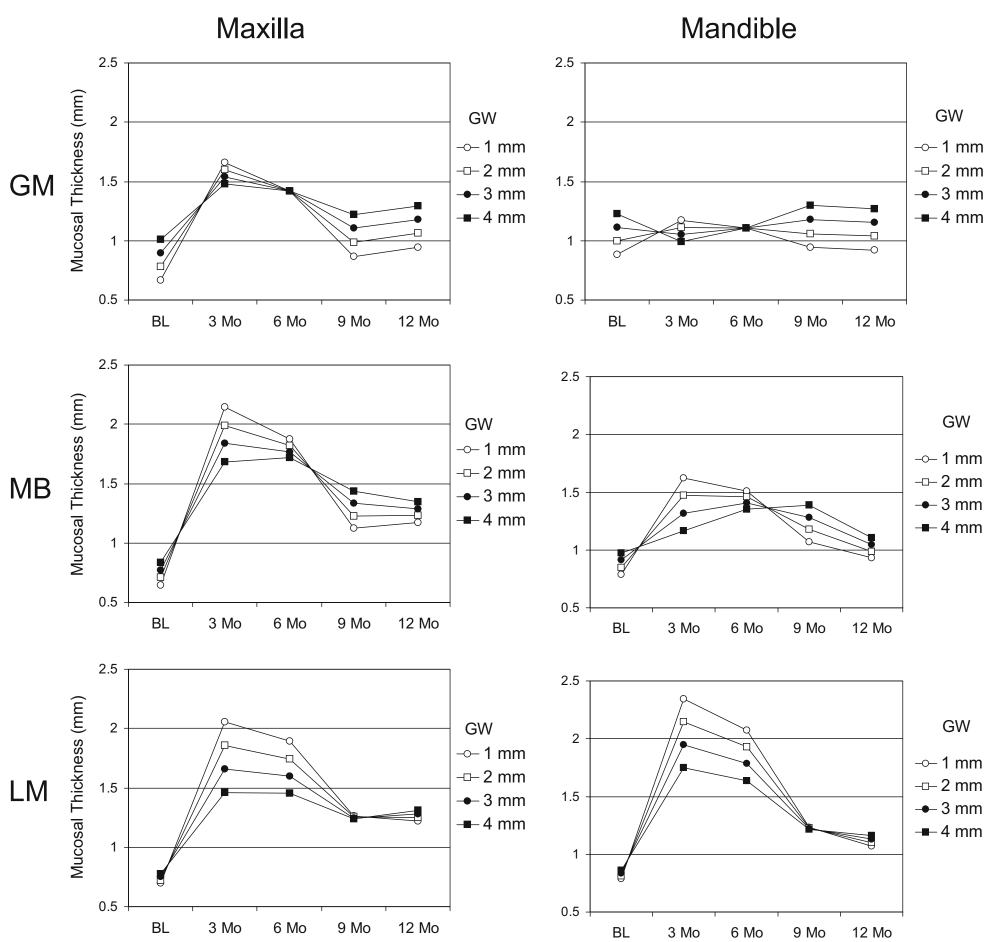

Fig. 2 Estimates of mucosal thickness derived from the multivariate, two-level time series model in Table 2. Thickness as measured at the gingival margin (*GM*), at the mucogingival border (*MB*), and of the lining mucosa (*LM*) in relation to time (baseline [*BL*] and at 3-month follow-up examination intervals after surgery, 3–12 months), jaw, and baseline gingival width (*GW*)

Table 4 Bivariate, two-level "best-fit" model for responses change and mean of recession after surgical root coverage

	Parameter	Change	Mean
Fixed part	Intercept $\beta_{0,1,jk}$	−2.065 (0.363)	1.621 (0.814)
	Recession width		0.417 (0.085)
	True dehiscence	0.321 (0.086)	
	Gingival thickness[a]		−1.158 (0.665)
	Canine	−0.556 (0.216)	−0.548 (0.152)
Random part			
Subject level	$\sigma^2_{v0,1}$	0.389 (0.218)	1.357 (0.565)
	σ_{v01}	−0.432 (0.273)	
Tooth level	$\sigma^2_{u0,1}$	0.298 (0.100)	0.126 (0.045)
	σ_{u01}	0.027 (0.049)	

Note that the lowest level defines the multivariate structure. Parameter estimates with standard error in parentheses
[a] As measured at the mucogingival border

Discussion

The dimensions of gingival tissues as possible predictors for postsurgical outcomes have attracted considerable attention. The current literature has been systematically reviewed by Hwang and Wang [7]. The thickness of the masticatory mucosa has more recently been measured by numerous authors for very different purposes [3, 4, 16, 13, 22, 29, 30]. It had been shown that gingival width and thickness might be permanently increased by the use of connective tissue grafts for surgical root coverage [14]. Guided tissue regeneration, on the other hand, did not result in relevant alterations of gingival dimensions [15, 18].

Despite being a very heterogeneous consortium of various epithelia and very different soft and hard connective tissues, the periodontium has traditionally been described as a biological, functional, and developmental unit [19]. Surgical interventions aiming at alterations of one component may inevitably affect other parts of this consortium as well. In addition, rebound effects are to be expected. Certain observations made in the present longitudinal study on the dimensions of the mucosa after surgical intervention for root coverage have already been described in a previous paper [15], where it was concluded that the implantation of a bio-absorbable membrane led to a largely transient thickening of both gingiva and lining mucosa. Furthermore, the surgical procedure itself involving guided tissue regeneration was tooth- and defect-type sensitive with best results (in terms of per cent root coverage) obtained at canines and in rather shallow recessions. Attachment gain seemingly depended on the depth of the lesion and was most pronounced at maxillary canines [15].

In the present revision of the data, a far more analytical approach was employed. While this study did not involve a control group, a particular strength of the present data is that clinical features of the gingival unit of a particular tooth had been investigated longitudinally in great detail. Quite advanced diagnostic means were employed, such as a pressure-controlled automatic probe, calipers, and an ultrasound device for the biometrical measurements, all with a 0.1-mm readout. All measurements were replicated in a second round and averaged to enhance reliability [15]. On the other hand, a limitation of this study is the rather small number of treated recession sites requiring confirmation of observations in further studies, where the influence of different types of recessions (for instance, Miller classes) should be analyzed in more detail. The small sample size most probably prevented the detection of significant effects in the present study.

Since the number of treated recession sites varied among patients, respective observations cannot be regarded independent [8]. Repeated observations are nested in teeth, which in turn are nested in patients. Thus hierarchical or multilevel modeling would be a natural approach of analyzing the data. Variance partition in unadjusted time series models revealed that most of the variance of gingival thickness, its width, and the location of the mucogingival border relative to the cemento-enamel junction could still be found at the occasion level. Gingival width did not change after surgery, while gingival thickness and the location of the mucogingival border underwent considerable shifts with time including significant linear (velocity), quadratic (deceleration), and cubic terms. A more elaborate, multivariate, time series model with mucosal thickness at all three measurement locations as response variables, which was adjusted for baseline gingival width and jaw, and respective interactions with time allowed the calculation of predictions over time. Predictions, as seen in Fig. 2, indicate different patterns for teeth in the maxilla and in the mandible. Moreover, gingival thickness was positively correlated at baseline and again after 9 and 12 months, with baseline gingival width. The considerable swelling of mucosa at all maxillary measurement locations and of lining mucosa in the mandible 3 months after surgery was, however, negatively related to baseline gingival width. The random part of the model yielded significant correlations between mucosal thickness measurements at the different locations.

That gingival thickness as measured at the gingival margin is closely related to gingival width has been shown in previous publications [5, 16]. The influence was less apparent or disappeared when mucosal thickness was measured at or apical to the mucogingival border. It is interesting to note that interactions of gingival width with time were highly significant for all three locations. Thus, the observed swelling of the tissue 3 months after surgery was more pronounced in case of shallow gingiva at baseline. This is in accordance with differences in composition of the connective tissue of gingiva and alveolar lining mucosa, only the latter tissue consisting of a distinctive submucosa with a loose arrangement of collagen and elastic fibers [20]. Notably, gingival thickness in the mandible did not change to that extent, in particular when measured at the gingival margin. The reasons for the different response in the mandible are not very clear. It might be speculated that marginal gingiva was thicker in the mandible at the outset (Fig. 2), which might have prevented it from further swelling after surgery. Further studies are required for confirmation of this observation.

Predictions showed that new tissue had been created 9 months after surgery mainly at maxillary teeth, and the situation seems to have stabilized at that point of time already. The amount of new tissue, for example at maxillary teeth, may be estimated from the predicted 0.3–0.5-mm increase in thickness. The observation of an increased thickness of lining mucosa may point to the flattening of the vestibular fold after coronal displacement of the flap for root coverage. The predicted location of the mucogingival border (see Table 1) was, after 9 and 12 months, about 0.9 mm (0.3, 1.5 mm) coronal to its baseline level.

While the present study design was chosen to describe surgically induced dimensional changes of the gingival unit, the primary outcome in comparable studies is usually root coverage. In the previous paper [15], two linear regression models were presented. In one model, clinical attachment gain (the difference between pre- and postsurgical attachment level) was regressed on a number of covariates including baseline recession. Since former contains in part the latter, indirect mathematic coupling is present [2, 24, 26]. In the other model, a ratio term, the percent root coverage, was used as the response. Using the ratio of the difference between pre- and postsurgical recession depth and baseline recession as the response variable inevitably gives rise to spurious results due to inappropriate model specification by violating essential model assumptions and mathematic coupling as well [28]. In the present reanalysis, recession was modeled using a recently described bivariate model of change and mean of pre- and postsurgical recession, which avoids mathematic coupling [12]. In contrast to a statement of the previous article [15], deeper sites did not yield better results in terms of root coverage.

Problems with mathematic coupling in regression analysis can be found in numerous recent articles on periodontal treatment results [9, 14, 15, 23, 31]. Frequently made statements such as “the deeper the baseline defect the better the postoperative outcome” are especially suspicious when derived from models where change is regressed on baseline value, a classical algebraic coupling of the two variables. It should be kept in mind that any covariate should be critically appraised for direct or indirect mathematical coupling before introducing it into the model.

In conclusion, multilevel modeling revealed that surgical root coverage employing a bio-absorbable membrane yielded the creation of significant amounts of new soft tissue in particular at maxillary teeth, which can be related to an observed average 0.3- to 0.5-mm increase in thickness of the mucosa after 12 months. The difference in pre- and postsurgical recession is strongly influenced by tooth type and the “true” bony dehiscence.

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