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Periodontal inflamed surface area: quantifying inflammatory burden

Willem Nesse[1], Frank Abbas[2], Ids van der Ploeg[2], Frederik Karst Lucien Spijkervet[1], Pieter Ubele Dijkstra[1,3,4] and Arjan Vissink[1]

[1]Department of Oral and Maxillofacial Surgery; [2]Department of Periodontology, Center for Dentistry and Oral Hygiene; [3]Center for Rehabilitation; [4]Graduate School for Health Research, of the University of Groningen and University Medical Center, Groningen, The Netherlands

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Abstract

Background: Currently, a large variety of classifications is used for periodontitis as a risk factor for other diseases. None of these classifications quantifies the amount of inflamed periodontal tissue, while this information is needed to assess the inflammatory burden posed by periodontitis.

Aim: To develop a classification of periodontitis that quantifies the amount of inflamed periodontal tissue, which can be easily and broadly applied.

Material and Methods: A literature search was conducted to look for a classification of periodontitis that quantified the amount of inflamed periodontal tissue. A classification that quantified the root surface area affected by attachment loss was found. This classification did not quantify the surface area of *inflamed* periodontal tissue, however. Therefore, an Excel spreadsheet was developed in which the periodontal inflamed surface area (PISA) is calculated using clinical Attachment Level (CAL), recessions and bleeding on probing (BOP).

Results: The PISA reflects the surface area of bleeding pocket epithelium in square millimetres. The surface area of bleeding pocket epithelium quantifies the amount of inflamed periodontal tissue. A freely downloadable spreadsheet is available to calculate the PISA.

Conclusion: PISA quantifies the inflammatory burden posed by periodontitis and can be easily and broadly applied.

Key words: inflammatory burden; periodontal inflamed surface area, PISA; periodontitis

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Periodontitis is a chronic inflammatory disease of the supporting tissues around the teeth. Severe generalized periodontitis affects 5–15% of any population worldwide and is a major cause of teeth loss (Yoshida et al. 2001, Al-Shammari et al. 2005, Burt 2005). Periodontitis may, however, affect more than teeth and their surrounding structures. Periodontitis is claimed to be a risk factor for a broad range of diseases such as cardiovascular diseases and stroke (Janket et al. 2003, Scannapieco et al. 2003a, Khader et al. 2004, Bahekar et al. 2007) diabetes (Saremi et al. 2005, Khader et al. 2006), pneumonia (Scannapieco et al. 2003b) and preterm low birth weight (Scannapieco et al. 2003c, Khader & Ta'ani 2005).

The biological model for the plausibility of periodontitis as a risk factor for other diseases holds that periodontitis causes an inflammatory burden by eliciting bacteraemia (Chiu 1999, Madianos et al. 2001), systemic inflammatory responses (Kweider et al. 1993, D'Aiuto et al. 2004, Beck et al. 2005, Montebugnoli et al. 2005, Southerland et al. 2006), or cross-reactivity leading to auto-immune reactions (Rosenstein et al. 2004, Bartold et al. 2005). This inflammatory burden in turn causes damage to the human body far beyond the oral cavity. Following this biological model, the larger the amount of inflamed periodontal tissue is, the larger the chances are of periodontitis eliciting bacteraemia, systemic inflammatory responses or cross-reactivity. Therefore, any classification of periodontitis as a risk factor for other diseases should quantify the amount of inflamed periodontal tissue in order to quantify the inflammatory burden.

Many studies express periodontitis as a non-continuous variable. These

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studies use cut-off points to classify patients as being either *un*affected or *a*ffected by mild, moderate or severe periodontitis. By definition, these classifications do not quantify the amount of inflamed periodontal tissue (Janket et al. 2003, Scannapieco et al. 2003a, b, c, Khader et al. 2004, Khader & Ta'ani 2005, Khader et al. 2006, Bahekar et al. 2007, Merchant & Pitiphat 2007). Some studies linking periodontitis to other diseases do quantify periodontitis as a continuous variable, i.e. using mean probing pocket depth (PPD) or mean clinical attachment level (Janket et al. 2003, Scannapieco et al. 2003a, b, c, Khader et al. 2004, Khader & Ta'ani 2005, Khader et al. 2006, Bahekar et al. 2007, Merchant & Pitiphat 2007). Although these are continuous variables, this does not necessarily mean that these outcome measures quantify the amount of inflamed periodontal tissue. Thus, none of the classifications currently used expresses periodontitis as a continuous variable that is a measure of the amount of inflamed periodontal tissue. Hence these classifications may not quantify the inflammatory burden posed by periodontitis.

In addition, a great variety of classifications is used. In research on periodontitis as a risk factor for preterm low birth weight for example, 13 different classifications of periodontitis are being used (Scannapieco et al. 2003c, Khader & Ta'ani 2005, Vettore et al. 2008). Broad application of just one classification of periodontitis would allow for a better comparison of these studies, which may in turn provide decisive conclusions on periodontitis as a risk factor for other diseases.

The goal of this paper was to develop a classification of periodontitis that quantifies the amount of inflamed periodontal tissue and which can be easily and broadly applied.

Material and Methods

Periodontal inflamed surface area (PISA)

Because no gold standard for periodontitis as a risk factor for other diseases exists, a list of demands was assembled for the construction of a new classification of periodontitis. The first and foremost demand was that the new classification should adequately quantify the amount of inflamed periodontal tissue. Second, the classification should be easy to use and broadly applicable. This means that the classification should make use of clinical measurements commonly used to establish periodontitis, i.e. Clinical attachment level (CAL), recession and bleeding on probing (BOP) measurements. A literature search was performed to look for a classification of periodontitis that met these demands.

A classification that quantified the total surface area of attachment loss was found (Hujoel et al. 2001). We will refer to this classification as the attachment loss surface area (ALSA). To calculate the ALSA, formulas were generated whereby linear probing measurements, from the cemento–enamel junction (CEJ) to the bottom of the pocket (i.e. CAL), around a particular tooth are transformed into the ALSA for that particular tooth (Despeignes 1979, Hujoel 1994, Hujoel et al. 2001).

The ALSA quantifies the root surface area that has become exposed due to attachment loss. However, the ALSA cannot be used to quantify the amount of inflamed periodontal tissue. ALSA does not quantify the periodontal epithelial surface area (PESA), because CAL instead of PPD measurements are used to calculate ALSA (Fig. 1). To calculate the PESA, the Recession Surface Area (RSA) has to be subtracted from ALSA (Fig. 1a and b). Since ALSA = PESA+RSA, it can be deducted that ALSA – RSA = PESA. To calculate the PESA there are three arithmetical possibilities, depending on the location of the gingival margin (LGM):

1. The LGM is below the CEJ so the RSA > 0. In this case, PPD < CAL and thus PESA < ALSA. Therefore PESA = ALSA – RSA (Fig. 1a).
2. The LGM is exactly at the CEJ. In this case, PPD = CAL, RSA = 0. Therefore PESA = ALSA (Fig. 1b).
3. The LGM is above the CEJ. Since PPD > CAL, PESA > ALSA. Using CAL will lead to an underestimation of PESA. Calculating the PESA is only possible by using PPD instead of CAL, i.e. entering PPD as CAL in the formula transforming linear measurements to surface area. This will still lead to an underestimation of PESA (Fig. 1c).

Thus, PESA accurately quantifies the surface area of pocket epithelium if LGM is at or below the CEJ. However, PESA does still not quantify the surface area of *inflamed* pocket epithelium. After all, the PESA also includes healthy pocket epithelium. Healthy pocket epithelium contains relatively few inflammatory cells and may pose an effective barrier against bacteria trying to enter the circulation (Amato et al. 1986, Thilo et al. 1986, Caton et al. 1988). Therefore, part of the PESA that consists of healthy epithelium may not contribute to the inflammatory burden.

The *inflamed* part of the PESA on the other hand, does theoretically pose an inflammatory burden. To calculate the inflamed part of the PESA we propose calculating part of the PESA that is affected by BOP. After all, BOP reflects decreased collagen density, increased blood vessel density and fragility and a reduction of epithelial thickness and epithelial integrity (Greenstein et al. 1981, Polson et al. 1981, Davenport et al. 1982, Muller-Glauser & Schroeder 1982, Amato et al. 1986). Thin, fragile or even discontinuous pocket epithelium, may serve as an entrance for oral bacteria into the systemic circulation. Furthermore, BOP is characterized by a dense infiltration of inflammatory cells (Thilo et al. 1986, Caton et al. 1988). These inflammatory cells may play a key role in eliciting a systemic inflammatory response or cross-reactivity. Thus, the bleeding surface area, the periodontal *inflamed* surface area (PISA), may be thought of as the main contributor to any systemic inflammatory burden posed by periodontitis. Therefore, the PISA is proposed as a classification of periodontitis that quantifies the amount of inflamed periodontal tissue and as such, quantifies the systemic inflammatory burden.

Results

Calculating PISA

Using the formulas described by Hujoel et al. (2001), a Microsoft Excel spreadsheet was constructed to facilitate PISA calculation. PISA is calculated in seven steps:

1. After filling in CAL measurements at six sites per tooth in the Excel spreadsheet, the computer calculates the mean CAL for each particular tooth.
2. The mean CAL around a particular tooth is entered into the appropriate formula for the translation of linear CAL measurements to the ALSA for that specific tooth (Hujoel et al. 2001).

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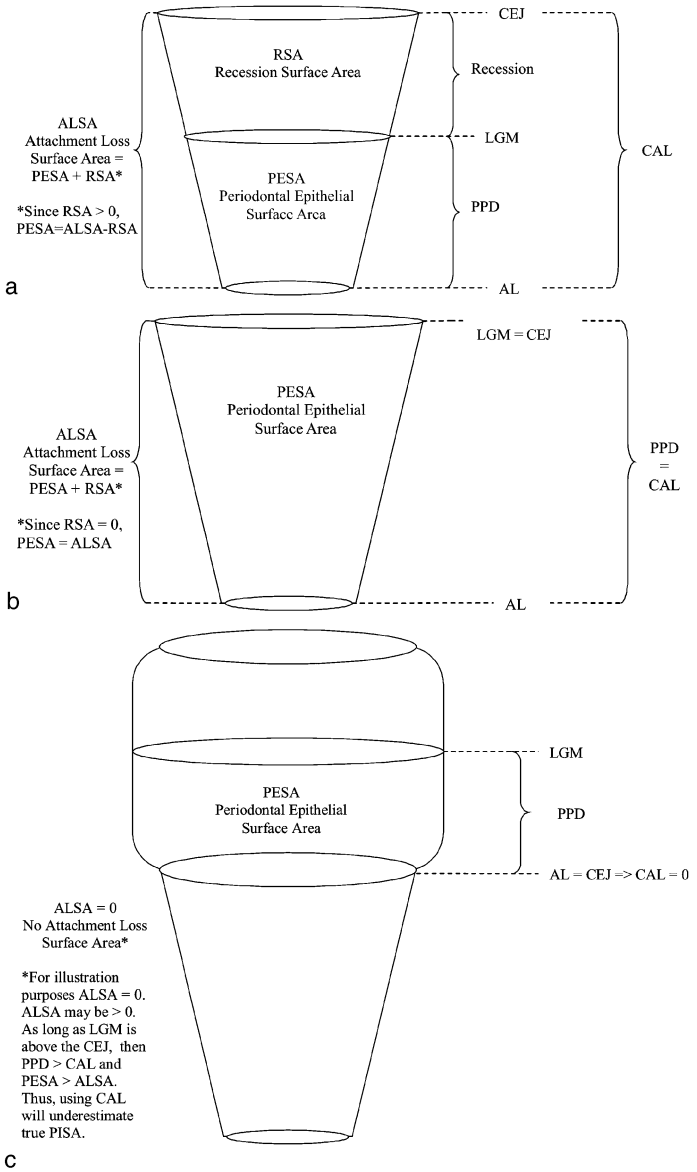

List of Abbreviations:
AL= Attachment Level; ALSA= Attachment Loss Surface Area; CAL= Clinical Attachment Level;
CEJ= Cemento-Enemal Junction; LGM= Location of Gingival Margin;
PESA= Periodontal Epithelial Surface Area; PISA= Periodontal Inflamed Surface Area;
PPD= Probing Pocket Depth, RSA= Recession Surface Area

Fig. 1. The location of the gingival margin determines how periodontal epithelial surface area is calculated.

3. After filling in recession measurements at six sites per tooth, the computer calculates the mean recession for each particular tooth.
4. The mean recession around a particular tooth is entered into the appropriate formula for the translation of linear recession measurements to the RSA for that specific tooth (Hujoel et al. 2001).
5. The RSA for a particular tooth is subtracted from the ALSA of that particular tooth, rendering the PESA for that specific tooth; i.e. PESA = ALSA – RSA (Fig. 1a and b).
6. The PESA for a particular tooth is then multiplied by the proportion of sites around the tooth that was affected by BOP. For example, if three out of the maximum of six sites were affected by BOP, the PESA of that particular tooth was multiplied by 3/6, thereby rendering the PISA for that specific tooth.
7. The sum of all individual PISAs around individual teeth is calculated, amounting to the total PISA within a patient's mouth.

Next, PISA was calculated for three different patients. Patient 1 has a healthy periodontium; exhibiting limited BOP with CAL not exceeding 3 mm (Fig. 2a). Patient 2 has severe local periodontitis; exhibiting BOP with CAL ranging from 6 to 10 mm locally (Fig. 2b). Patient 3 has severe generalized periodontitis, exhibiting widespread BOP with CAL ranging from 3 to 10 mm (Fig. 2c). PISA may thus range from 28.6 mm^2 ($\approx$0.3 cm^2) in healthy individuals to 3,899 mm^2 ($\approx$39 cm^2) in patients with severe generalized periodontitis (Fig. 2).

Spreadsheets are freely available from our website: www.parsprototo.info. All it takes to calculate PISA is filling in CAL, recessions and BOP on six sites per tooth in this freely downloadable spreadsheet. In addition to research purposes, the spreadsheet might also be used to show patients their surface area of bleeding pocket epithelium in millimetres square, illustrating the inflammatory burden periodontitis potentially poses to their body.

Discussion

The great variation in periodontal classifications used in the various studies and the lack of a tool that adequately assesses the inflammatory burden of periodontitis is a major drawback of the studies published on the periodontal inflammation–systemic disease interaction. Therefore, a new measure of periodontitis as a risk factor for other diseases was developed, the PISA. PISA reflects the surface area of bleeding pocket epithelium in square millimetres. PISA is calculated using conventional CAL, recession and BOP measurements. PISA quantifies the amount of inflamed periodontal tissue, thereby quantifying the inflammatory burden posed by periodontitis. A freely downloadable spreadsheet is available to calculate PISA, therefore PISA can be easily and broadly applied. Broad application of PISA may provide decisive conclusions on periodontitis as a risk factor for other diseases. An additional advantage of the PISA is that it can be retrospectively calculated using existing research data containing CAL, recession and BOP measurements.

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	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
CAL	buccal		3 2 3	3 2 3	3 2 3	2 1 2	3 1 3	2 1 2	2 1 2	2 1 2	2 1 2	2 2 2	2 1 2	2 1 2	3 2 3	3 2 3		buccal	CAL
	palatinal		3 2 3	2 2 3	3 2 3	3 2 2	3 2 3	3 2 2	2 2 3	3 2 2	2 2 2	2 2 3	3 2 2	2 2 3	3 2 2	3 2 3		palantinal	
	lingual		3 2 3	3 2 3	2 2 3	3 2 2	2 2 3	2 2 2	2 2 2	2 2 2	2 1 2	3 1 2	3 2 3	3 2 3	3 2 3	3 2 3		lingual	
CAL	buccal		3 2 2	3 2 3	2 1 2	2 1 2	2 1 2	2 1 2	2 1 3	3 1 2	2 1 2	2 1 2	2 2 2	2 2 2	2 2 2	2 2 3		buccal	CAL
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
LGM	buccal		0 0 0	0 0 0	0 0 0	0 1 1	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	1 2 0	0 0 0	0 0 0		buccal	LGM
	palatinal		0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		palantinal	
	lingual		0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		lingual	
LGM	buccal		0 0 0	0 0 0	0 0 0	0 0 0	1 2 1	0 0 0	0 0 0	0 0 0	0 0 0	2 2 0	0 0 0	0 0 0	0 0 0	0 0 0		buccal	LGM
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
ALSA (mm2)	0	77,47657	59,0216	70,75736	38,1438	47,8923	34,04481	28,71903	28,71903	31,31441	41,05673	38,1438	57,40454	59,0216	77,47657	0	ALSA (mm2)
(mm2) ALSA	0	26,28928	35,84653	39,49991	38,58749	39,70533	28,62673	30,45238	30,45238	26,03916	36,86338	44,29206	47,36757	28,55048	26,28928	0	(mm2) ALSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
RSA (mm2)	0	0	0	0	7,050607	0	0	0	0	0	0	0	17,95305	0	0	0	RSA (mm2)
(mm2) RSA	0	0	0	0	0	15,06533	0	0	0	0	15,06533	0	0	0	0	0	(mm2) RSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

tooth	PESA	nr of sites with BOP	PISA (mm2)
18	0		0
17	77,48	1	12,91
16	59,02		0
15	70,76		0
14	31,09		0
13	47,89		0
12	34,04		0
11	28,72		0
21	28,72		0
22	31,31		0
23	41,06		0
24	38,14		0
25	39,45	1	6,58
26	59,02		0
27	77,48		0
28	0		0

tooth	PESA	nr of sites with BOP	PISA (mm2)
38	0		0
37	26,29		0
36	28,55	1	4,76
35	47,37		0
34	44,29		0
33	21,8		0
32	26,04		0
31	30,45		0
41	30,45		0
42	28,63		0
43	24,64		0
44	38,59		0
45	39,5		0
46	35,85		0
47	26,29	1	4,38
48	0		0

Total **Periodontal Epithelial Surface Area** (mm2)
1112,9

Total **Periodontal Inflamed Surface Area** (mm2)
28,6

CAL = Clinical Attachment Level relative to CEJ
LGM = Location of Gingival Margin relative to CEJ
ALSA = Attachment Loss Surface Area
RSA = Recession Surface Area
PESA = Periodontal Epithelial Surface Area
PISA = Periodontal Inflamed Surface Area

a

	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
CAL	buccal		4 3 4	4 3 4	3 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 3	4 3 4	4 3 4		buccal	CAL
	palatinal		3 3 3	3 3 4	3 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 3 3	4 3 3	3 3 3		palantinal	
	lingual		5 5 6	5 3 4	5 3 4	3 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 4	5 6 8	10 8 9	7 7 8		lingual	
CAL	buccal		4 3 4	4 3 5	4 4 3	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	2 2 2	4 2 4	5 5 6	8 8 7	8 8 10		buccal	CAL
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
LGM	buccal		0 0 0	0 0 0	0 0 0	0 0 0	0 1 2	2 3 2	2 2 3	3 2 2	2 1 0	0 0 0	0 1 2	1 0 0	0 0 0	0 0 0		buccal	LGM
	palatinal		0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		palantinal	
	lingual		0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		lingual	
LGM	buccal		0 0 0	0 0 0	0 2 1	1 2 2	3 3 2	0 0 0	0 1 2	2 1 0	0 0 0	0 2 3	2 1 0	0 0 0	0 0 0	0 0 0		buccal	LGM
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
ALSA (mm2)	0	101,004	102,5321	64,29466	38,1438	37,66208	34,04481	28,71903	28,71903	34,04481	37,66208	38,1438	67,57394	102,5321	101,004	0	ALSA (mm2)
(mm2) ALSA	0	108,6176	79,91301	82,67267	41,43582	39,70533	31,22813	30,45238	30,45238	31,22813	39,70533	55,91504	124,7817	275,6647	278,5708	0	(mm2) ALSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
RSA (mm2)	0	0	0	0	0	8,638211	20,34225	15,4635	15,4635	9,027744	0	10,41922	6,347211	0	0	0	RSA (mm2)
(mm2) RSA	0	0	0	7,728455	17,92883	28,01661	0	9,342187	9,342187	0	18,4641	11,29398	0	0	0	0	(mm2) RSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

tooth	PESA	nr of sites with BOP	PISA (mm2)
18	0		0
17	101	2	33,67
16	102,5	4	68,35
15	64,29	2	21,43
14	38,14		0
13	29,02	1	4,84
12	13,7	1	2,28
11	13,26		0
21	13,26		0
22	25,02		0
23	37,66		0
24	27,72	1	4,62
25	61,23	1	10,20
26	102,5	2	34,18
27	101	2	33,67
28	0		0

tooth	PESA	nr of sites with BOP	PISA (mm2)
38	0		0
37	278,6	6	278,57
36	275,7	6	275,66
35	124,8	4	83,19
34	44,62	3	22,31
33	21,24		0
32	31,23		0
31	21,11		0
41	21,11		0
42	31,23		0
43	11,69		0
44	23,51	1	3,92
45	74,94	3	37,47
46	79,91	6	79,91
47	108,6	3	54,31
48	0		0

Total **Periodontal Epithelial Surface Area** (mm2)
1878,6

Total **Periodontal Inflamed Surface Area** (mm2)
1048,6

CAL = Clinical Attachment Level relative to CEJ
LGM = Location of Gingival Margin relative to CEJ
ALSA = Attachment Loss Surface Area
RSA = Recession Surface Area
PESA = Periodontal Epithelial Surface Area
PISA = Periodontal Inflamed Surface Area

b

Fig. 2. (a) Full mouth clinical attachment level (CAL), recession and bleeding on probing (BOP) measurements on six sites per tooth from a healthy patient. The periodontal epithelial surface area (PESA) is 1,112.9 mm^2 ($\approx$11 cm^2), the PISA is 28.6 mm^2 ($\approx$0.3 cm^2). (b) Full mouth CAL, recession and BOP measurements on six sites per tooth from a patient with severe localized periodontitis. The PESA is 1,878.6 mm^2 ($\approx$19 cm^2), the PISA is 1,048.6 mm^2 ($\approx$10 cm^2). (c) Full mouth CAL, recession and BOP measurements on six sites per tooth from a patient with severe generalized periodontitis. The PESA is 3,899.1 mm^2 ($\approx$39 cm^2), the PISA is 3,704.2 mm^2 ($\approx$37 cm^2).

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	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
CAL	buccal		9 6 7	8 6 10	8 5 6	6 5 6	6 5 4	4 3 4	6 4 7	7 4 5	4 3 4	4 5 6	6 5 6	6 5 8	9 7 8	7 6 9		buccal	CAL
	palatinal		8 6 8	9 7 9	6 5 5	5 4 4	5 3 5	3 3 3	6 4 5	4 3 4	3 3 3	5 3 5	4 4 5	5 5 6	9 7 9	8 6 8		palantinal	
	lingual		9 6 8	9 5 9	8 4 6	6 5 5	6 3 7	6 3 4	5 3 4	5 3 5	4 4 5	6 4 6	5 5 6	6 4 8	9 5 9	8 6 9		lingual	
CAL	buccal		9 5 8	6 4 9	7 3 6	6 3 5	5 3 4	4 3 4	4 3 5	4 3 4	4 4 4	5 3 4	5 3 5	6 3 7	9 4 6	8 5 9		buccal	CAL
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

	tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth	
LGM	buccal		2 1 0	0 0 0	0 0 0	0 0 0	0 2 2	3 2 0	0 0 0	0 0 0	1 2 1	0 0 0	0 0 0	0 0 0	0 0 0	1 3 3		buccal	LGM
	palatinal		2 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 3		palantinal	
	lingual		0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0		lingual	
LGM	buccal		2 1 0	0 0 0	0 0 0	0 0 0	0 0 1	2 2 3	3 2 2	2 3 2	2 2 2	1 0 0	0 0 0	0 0 0	0 0 0	1 2 3		buccal	LGM
	tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth	

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
ALSA (mm2)	0	309,965	389,9383	121,3678	95,01119	92,12413	56,11295	95,77463	78,35939	56,11295	92,12413	95,01119	121,3678	389,9383	309,965	0	ALSA (mm2)
(mm2) ALSA	0	264,0732	222,4091	121,568	90,05669	83,83873	63,67829	61,59537	61,59537	66,4468	83,83873	90,05669	121,568	222,4091	264,0732	0	(mm2) ALSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

tooth	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	tooth
RSA (mm2)	0	23,03762	0	0	0	11,66443	14,75559	0	0	11,91364	0	0	0	0	47,04186	0	RSA (mm2)
(mm2) RSA	0	14,46263	0	0	0	4,020051	18,3305	19,17812	19,17812	15,76584	4,020051	0	0	0	17,88605	0	(mm2) RSA
tooth	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	tooth

C

tooth	PESA	nr of sites with BOP	PISA (mm2)
18	0		0
17	286,9	6	286,93
16	389,9	6	389,94
15	121,4	6	121,37
14	95,01	5	79,18
13	80,46	4	53,64
12	41,36	4	27,57
11	95,77	6	95,77
21	78,36	6	78,36
22	44,2	4	29,47
23	92,12	5	76,77
24	95,01	5	79,18
25	121,4	6	121,37
26	389,9	6	389,94
27	262,9	6	262,92
28	0		0

tooth	PESA	nr of sites with BOP	PISA (mm2)
38	0		0
37	246,2	6	246,19
36	222,4	6	222,41
35	121,6	5	101,31
34	90,06	6	90,06
33	79,82	5	66,52
32	50,68	4	33,79
31	42,42	5	35,35
41	42,42	4	28,28
42	45,35	5	37,79
43	79,82	5	66,52
44	90,06	6	90,06
45	121,6	6	121,57
46	222,4	6	222,41
47	249,6	6	249,61
48	0		0

Total **Periodontal Epithelial Surface Area** (mm2)
3899,1

Total **Periodontal Inflamed Surface Area** (mm2)
3704,2

CAL = Clinical Attachment Level relative to CEJ
LGM = Location of Gingival Margin relative to CEJ
ALSA = Attachment Loss Surface Area
RSA = Recession Surface Area
PESA = Periodontal Epithelial Surface Area
PISA = Periodontal Inflamed Surface Area

Fig. 2. Continued.

Although PISA is thought to be the best tool for assessment of the amount of periodontal inflamed tissue that is currently available, for several reasons PISA might not *precisely* quantify the amount of inflamed tissue. First, CAL, recession and BOP measurements used for the calculation of PISA always include measurement errors related to observer, instrument, teeth patients and their interactions. Second, the formulas transforming CAL and recession to surface area, use population-based mean values of both root surface areas and root lengths. Thus, individual variations in root surface area and root length are not taken into account when calculating PISA. Third, PISA quantifies the amount of inflamed periodontal tissue in *two* dimensions, whereas in fact periodontitis is a *three* dimensional inflammatory process, i.e. extending into the connective tissue around the root. For these reasons, PISA may not *precisely* quantify the amount of inflammatory tissue. However, PISA likely quantifies the amount of inflamed periodontal tissue for each individual patient more accurately than any classification currently used.

PISA is, however, unable to accurately quantify the amount of inflamed periodontal tissue in case of pseudopockets or gingival overgrowth, i.e. when the gingival margin is located above the CEJ (Fig. 1c). In these cases, CAL will be smaller than PPD and ALSA will consequently be smaller than PESA. Therefore, using only CAL will underestimate the true PESA and thereby underestimate true PISA. Using PPD instead of CAL, i.e. entering PPD into the formula for CAL, will diminish this underestimation. However, given the conical shape of a root, it will still lead to a slight underestimation of true PISA. Fortunately, cases of gingival overgrowth are relatively rare, and often due to usage of mediation (e.g. anti-epileptic drugs, immune suppressive drugs, calcium blockers) or presence of certain diseases (e.g. leukaemia). These cases are not representative for the general population. Therefore, PISA can be used in the majority of cases, i.e. when the gingival margin is located at or below the CEJ. In case the gingival margin is located above the CEJ, PISA might still be used by replacing CAL with PPD, taking into account that it will result in an underestimation of true PISA.

Finally, PISA might not adequately predict the probability of periodontitis to cause other diseases, even if it would be possible to measure precisely the amount of inflamed periodontal tissue. For example, the *type* of inflammation might be more important in causing other diseases than the *amount* of inflammation. Certain cells, proteins or inflammatory mediators might play a key role in causing other diseases. Furthermore, there might be a critical level of inflammation that functions as a threshold. When the threshold is passed, a response is initiated that causes damage to the human body beyond the oral cavity. Finally, PISA does not take into account the type of microbiological flora. Certain oral micro organisms might play a key role in causing other diseases, e.g. *Campylobacter rectus*, *Prevotella intermedia*, *Porphyromonas gingivalis* and *Peptostreptococcus micros* (Chiu 1999, Madianos et al. 2001, Beck et al. 2005). For these reasons, the PISA might not be the only determinant in predicting the probability of periodontitis to cause other diseases. When additional information on the role of certain inflammatory mediators or microorganisms in causing other diseases becomes available, this information and the PISA can be incorporated in a new model that predicts the probability of periodontitis to cause other diseases even more accurately.

Although the PISA still has shortcomings, theoretically it appears to be a far better classification of periodontitis as a risk actor for other diseases than any classification currently used (face validity). The next step is to perform studies to analyse construct validity by means of correlating PISA with

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measures of the activity, severity or presence of other diseases.

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Address:
W. Nesse
Department of Oral and Maxillofacial Surgery
University of Groningen and University Medical Center
PO Box 30.001
9700 RB Groningen
The Netherlands
E-mail: w.nesse@kchir.umcg.nl

Clinical Relevance

Scientific rationale for the study: Currently, all classifications of periodontitis fail to quantify the amount of inflamed periodontal tissue, while this may be the link between periodontitis and other diseases.

Principal findings: The PISA reflects the surface area of bleeding pocket epithelium in millimetres square, thereby quantifying the probability of periodontitis to cause other diseases.

Practical implications: A freely downloadable spreadsheet is available to calculate PISA using CAL, recession and BOP measurements. This spreadsheet can be used to show patients their surface area of bleeding pocket epithelium, illustrating the inflammatory burden periodontitis potentially poses to their body.

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