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A Simple Mathematical Model for Wound Closure Evaluation

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Abstract The incidence of ulcers associated to type 2 diabetes mellitus (T2DM) increases every year. We introduce and explore a new mathematical algorithm to evaluate wound-healing in foot ulcers associated to T2DM. Fifteen patients (nine women and six men), mean age of 70 ± 16 years were included. The evolution of their wounds followed-up for a period of 18–45 days. According to the Wagner grading system the ulcers were grade I (5 patients), grade II (9 patients), and grade III (1 patient). Clinically, the type of the ulcers was neuroischemic (12 patients) and neuropathic (3 patients). A new parameter is introduced, the "continuous linear healing rate" Dc that was more accurate with higher values and requires less quantifications than usual formulas to make a wound-healing projection.
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Introduction

Wound-healing is a complex biological process that involves the expression of growth factors that promote various cellular processes, production of new connective tissue matrix, and collagen deposition.[1] Studies have shown that it is possible, under appropriate treatments, to achieve wound closure in about 45 days.

Decision-making by nurses and physicians during wound-healing may be difficult due to lack of quantitative criteria which allow an accurate diagnosis of the quality of the wound progression. With the presence of a pool of protocols and products possessing the potential to improve wound progression to closure, the selection of one of these may become arbitrary. In order to perform quantitative

analyses, data acquisition must be carried out, which adds another difficulty to the work of the clinical staff. Data acquisition should be simple and fast to be easily incorporated into healing protocols by nurses. In addition, data treatment and interpretation must not involve complicated protocols; either demand high qualification in disciplines other than medical, such as mathematics, physics, or computation. Stochastic models[2] that consider delayed exponential behavior,[3] or photogrammetric software,[4] furnish reliable methods on the evaluation of diabetic foot ulcers, but the protocols, in terms of algorithms and the software required, may result sufficiently complicated to minimize their use by nurses in hospitals and family health centers, where treatments are normally performed.

Evidence showed that monitoring healing progression for 2 or 4 weeks may serve to predict eventual wound closure under appropriate mathematical models.[5] Mathematical modeling may also aid in identifying potential methods for disease control and management if wound closure results can be correlated with the wound and the patient's condition.[6] Few mathematical models in the literature deal with the complications associated with diabetes due to their complexity.[6] The literature reveals great diversity in the procedures employed to compare wound-healing rates, including variables such as periods of study, type, size and shape of the analyzed lesions, closing rate definition, calculation methods, mechanisms, etc.[3,7–13] However, controversy exists in the selection of the adequate indicative parameter of the wound closure rate.[8,9,14,15] Assessment of wound status in terms of time is often based on measurements of wound area and, to a lesser extent, of the wound perimeter[8,14–17] and the linear healing rate (D) has been often utilized. The D parameter is obtained through a method of calculation based on differences; thus, accurate calculation requires a large number of data to achieve statistical significance. However, the concept of linear healing involves a constant, perpendicular advance of the wound margin toward the wound's open area, and this feature may be used to propose a mathematical development based on differentials.

The aim of this study is to introduce and test a mathematical algorithm for calculation of wound-healing rate from few clinical data obtained by monitoring wound closure in patients with Type 2 Diabetes Mellitus (T2DM).

Materials and Methods

The research study protocol was approved by the Ethics Committee of the Medical Sciences Research Center (CICMED), Autonomous University of the State of Mexico (UAEMex). The investigation conforms to the principles in the Declaration of Helsinki, and the patients were fully informed regarding the aim of the study and signed written informed consent.

This was a bi-center, open-label, phase I, descriptive study. A total of 15 consecutive patients with T2DM and foot ulcer up to grade III on the Wagner scale were enrolled in this study. Patients were recruited at the Healing Ulcer Service, Clínica 251, Instituto Mexicano del Seguro Social (IMSS), Metepec, Estado de México (3 patients), and at the Clínica de Consulta Externa "Alfredo del Mazo Vélez," ISSEMyM, Toluca, Estado de México (12 patients) between September 2012 and August 2013. Other subjects who had clinical signs of severe infection and those unwilling to participate in the study were excluded.

Clinical Follow-up

Age, gender, duration of diabetes, time of wound evolution, Wagner ulcer grade, and vascular status were recorded for all patients. The ulcer was delineated for each patient on a sterile acetate sheet, and a scale was added. Images were digitized and analyzed with AutoCAD 2009 software to determine their area and perimeter. Five or more measurements were carried out at the beginning of the study and during follow-up for 18–45 days. Patients were advised to have their dressing changed daily, either at the outpatient clinic of our hospital, at a nearby local hospital, or with the aid of the community nurse who provided home care for patients with ambulatory problems.

Mathematical Model

According to Gilman,[8] we can define the linear healing rate (D) as follows:

$$D = -\frac{\Delta A}{P_{avg}\Delta t} \tag{1}$$

where ΔA is the change in superficial wound area between 2 consecutive clinic visits, Δt is the time between the two visits, and P_{avg} is the average wound perimeter measured at the two clinic visits. This equation is evaluated in discrete times during the wound-healing process, normally once a week, and the final value is averaged among the discrete values obtained at each discrete time, obtaining the average D value (D_{avg}). The drawback of this method is that in order to obtain statistical significance, a large number of visits and data acquisitions are needed, and data frequently exhibit great dispersion.

However, the concept of linear healing involves a regular advance of the wound contour toward the wound open area and perpendicular to the wound margin; thus, data corresponding to this magnitude are theoretically linked with each other by a linear trend over time. This concept may be mathematically formulated by considering the effective advance of the wound margin during an infinitely small period of time (Fig. 1). Thus, the continuous linear healing rate (D_c) can be defined as:

$$D_c = \lim_{\Delta t \to 0} D = \lim_{\Delta t \to 0} -\frac{\Delta A}{P_{avg} \Delta t} = -\frac{dA}{Pdt} = -\frac{dr}{dt} \quad (2)$$

where A: area, d: delta, lim: limit, P: perimeter, P_{avg}: average wound perimeter measured at two clinic visits, r: length perpendicular to the wound contour, ΔA: change in superficial wound area between 2 consecutive clinic visits, Δt: time between two visits. $dA = \lim DA$ when DA approaches 0.

Considering that according to Fig. 1:

$$dA = Pdr \quad (3)$$

where A is superficial wound area, r is the length perpendicular to the wound contour, and P is the wound perimeter.

Then, it is clear that $dA = -PD_c dt$ (4)

Integration of equation (4) leads to

$$\frac{A}{P} = -D_c t + q \quad (5)$$

where q is the intercept, denoting the extrapolated A/P initial values. Plotting A/P vs. time, the values of D_c and q can be obtained from the slope and the ordinate at the origin, respectively. Basically, q contains information on the aspect of the wound, such as those comprising extrapolated A/P initial values. Because P and A have dimensions of length and square length, respectively, we can define the Shape coefficient (S_c) as:

$$S_c = \frac{P^2}{A} \quad (6)$$

This coefficient does not depend on the size of the analyzed figure, but on its shape, and may be an appropriate parameter for evaluating changes in the shape of a particular wound or differences among the shapes of different wounds. This assumes a value of 12.56 for circular wounds and 16 for square wounds, as depicted in Fig. 1.

In addition, equation (5) can be used to obtain projected time of wound closure ($t_{closure}$), a condition under which $A = 0$, so that:

$$t_{closure} = \frac{q}{D_c} \quad (7)$$

If we consider linear healing as a physiological fact, deviation from the linear trend following equation (5) should be caused by changes in the shape of the wound and other physiological conditions that may influence the value of D_c during wound-healing.

Statistical Analysis

STATISTICA version 8.0 software was utilized to analyze statistical correlations between variables; statistical differences by grouping patients by Wagner's grade of wound type were searched using the Mann–Whitney U test.

Results

Fifteen patients (nine females and six males) with a mean age of 70 ± 16 years were included in the study. According to the Wagner grading system, ulcers were grade I (5 patients), grade II (9 patients), and grade III (1 patient).
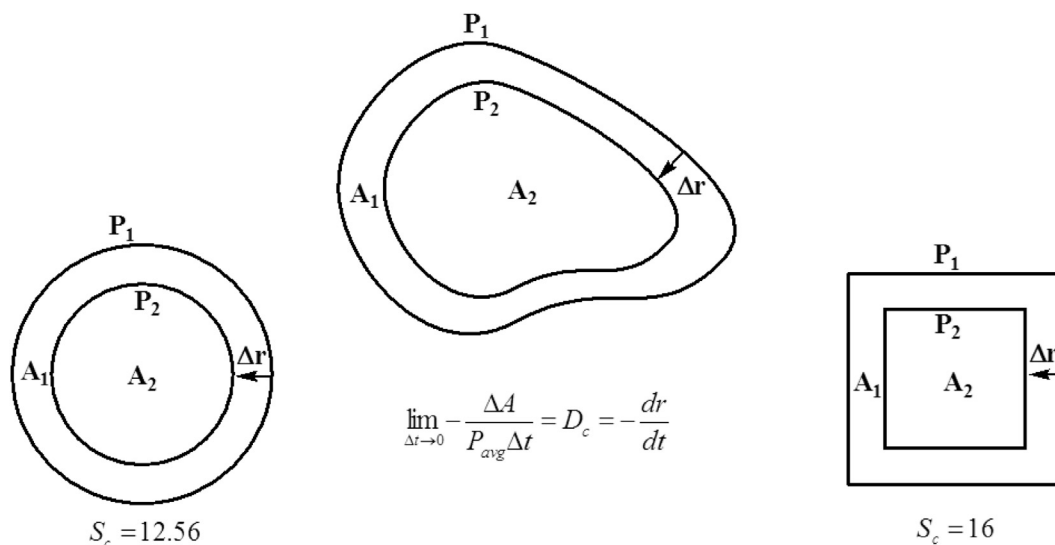
Figure 1   Wound evolution scheme for different shapes. A: area, D_c: continuous linear healing rate, lim: limit, P: perimeter, P_{avg}: average wound perimeter measured at two clinic visits, r: length perpendicular to the wound contour, S_c: shape coefficient, ΔA: change in superficial wound area between 2 consecutive clinic visits, Δt: time between two visits.

Table 1 Anthropometric and clinical characteristics of the patients.

Case	Gender	Age	Duration of diabetes (years)	Time with the ulcer (months)	Wagner stage	Wound type
P1	M	56	25	12	II	Neuroischemic
P2	F	62	4	2	II	Neuroischemic
P3	F	79	5	2	II	Neuroischemic
P4	F	91	26	3	II	Neuroischemic
P5	M	85	35	2	II	Neuroischemic
P6	M	71	6	6	III	Neuroischemic
P7	F	40	13	63	II	Neuroischemic
P8	M	74	14	4	I	Neuropathic
P9	F	97	18	5	I	Neuroischemic
P10	F	45	1	6	II	Neuroischemic
P11	M	75	5	8	II	Neuroischemic
P12	F	62	1.6	2	I	Neuropathic
P13	M	67	5	3	I	Neuroischemic
P14	F	66	2	1	I	Neuropathic
P15	F	81	8	5	II	Neuroischemic

F: female, M: male, P: patient.

Clinically, the ulcer type was neuroischemic (12 patients) and neuropathic (3 patients). Duration of ulcer evolution prior to treatment ranged between 1 and 63 months (Table 1).

Ulcer Healing

Data obtained from planimetric measurements have been treated introducing A, P, and t in equations (1), (5) and (6). D values obtained from equation (1) for the healing process of the 15 patients are shown in Fig. 2, as they are usually presented in the literature.[15]

The corresponding D_{avg} values are listed in Table 2, together with the corresponding values of the absolute and relative Standard Deviations (SD and RSD, respectively). D values of the same order of magnitude as those

usually reported were found.[17] However, in the majority of cases, corresponding RSD were >100% (Table 2), with an outstanding value close to 800% for patient (P) 14. RSD was used to evaluate the quality of the data for the D_{avg} calculation, and the high values found indicate low quality. In addition, there was no correlation between the D_{avg} value and RSD values ($r = 0.4834$; $p = 0.68$); therefore, the data dispersion for each patient was assumed to be independent from the healing rate. High dispersion of D values for each single patient makes it difficult to establish comparisons between patients.

On the other hand, utilizing the same raw data, D_c values have been obtained by means of equation (5) and are illustrated in Table 3. In order to obtain trends deriving from the same origin, A/P data and the corresponding linear adjustments have been plotted in Fig. 3 for all patients after
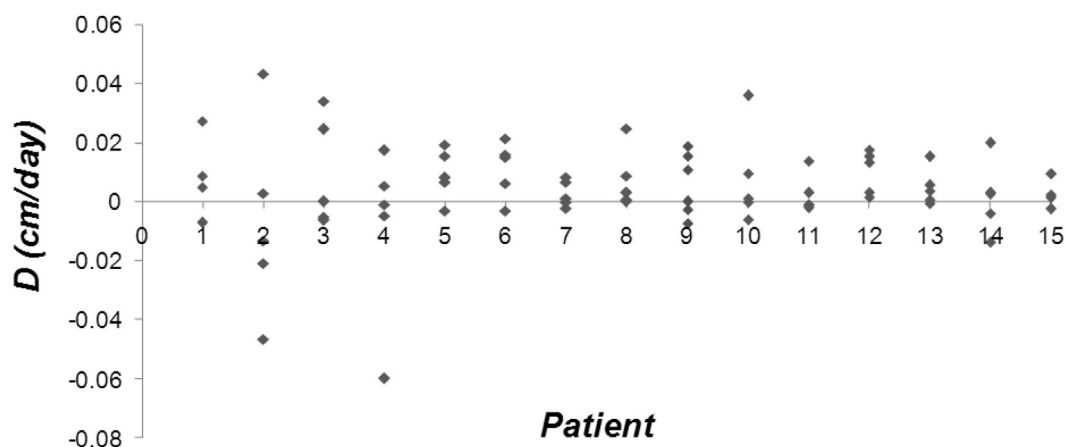
Figure 2 D (◆) for each patient. D: linear healing rate.

Table 2 D_{avg} and corresponding SD and RSD.

Patient	$D_{avg} \pm SD$ (cm/day)	RSD (%)
P1	0.00828 ± 0.01424	172
P2	−0.00701 ± 0.03318	473
P3	0.00939 ± 0.01858	198
P4	−0.00868 ± 0.02981	344
P5	0.00916 ± 0.00871	95
P6	0.01094 ± 0.00959	88
P7	0.00263 ± 0.00453	172
P8	0.00740 ± 0.01024	138
P9	0.00580 ± 0.01060	183
P10	0.00795 ± 0.01657	208
P11	0.00244 ± 0.00656	269
P12	0.01012 ± 0.00737	73
P13	0.00484 ± 0.00623	129
P14	0.00153 ± 0.01222	796
P15	0.00401 ± 0.00535	133

D_{avg}: average linear healing value, RSD: relative standard deviation, SD: standard deviation.

subtracting q. The resulting straight lines were distributed in a cone.

Expressions of linear adjustments of A/P vs. t and the corresponding R^2 values are also presented in Table 3. R^2 values were also used to evaluate data quality for calculation of D_c, based on the assumption of a linear behavior. R^2 values found presented values between 0 and 1. There was a positive correlation between D_c and R^2 ($r = 0.6384$; $p = 0.010$). Because this correlation was positive and statistically significant, we can conclude that higher D_c values resulted more accurate than lower values. One patient (P2) exhibited negative values of D_c, indicating that the wound was enlarging, and a very low value of R^2

was found (0.03). Six patients showed positive D_c values of <0.002 cm/day (P11, P9, P15, P14, P7, and P13), and the corresponding R^2 ranged between 0.22 and 0.60. Six patients demonstrated values of around 0.004 cm/day (P8, P12, P4, P1, P3, and P6), and the corresponding R^2 ranged between 0.24 and 0.96. Two patients showed D_c values of >0.006 cm/day (P10 and P5), and the corresponding R^2 were 0.62 and 0.95. Total wound closure should occur at $t_{closure}$ (extracted from equation (7)) whose values are shown in Table 3 for patients showing D_c values. The values obtained for $t_{closure}$ ranged between 52 and 805 days. The mean $t_{closure}$ value obtained for the patients was 260 days, and the data showed an SD of 212 (RSD, 81%).

In order to compare the results obtained from two different methods, D_c and D_{avg} values were plotted in Fig. 4a, where patient entries were ordered according to D_c values. In that D_c and D_{avg} were calculated from the same data, a positive correlation was expected between both magnitudes, which was statistically confirmed ($r = 0.5490$; $p = 0.034$). However, outstanding differences were found in P2 and P4. For P4, an inversion on the sign of the corresponding value was observed, because D_c was positive and D_{avg} was negative. In general, positive values of both magnitudes were found, with D_c lower than D_{avg}. In addition, there was no correlation between the corresponding R^2 (corresponding to the calculation of D_c by linear adjustment) and RSD corresponding to the calculation of D_{avg} ($r = 0.2267$; $p = 0.417$) (Tables 2 and 3). Notably, for patients exhibiting high values of R^2 when calculating D_c (>0.90), such as P1, P5, and P12, the RSD values found were still high and close to 100%.

Assays for observing any correlation between D_c or D_{avg} with wound shape and size have been conducted. In this

Table 3   Linear adjustments of A/P data versus t, D_c, S_c, and corresponding SD and RSD.

Patient	Linear adjustment (equation (6))	R^2	D_c (cm/day)	$S_c \pm SD$	RSD (%)	$t_{closure}$ (days)
P1	$y = -0.00396x + 1.25068$	0.96	0.00396	13.74 ± 0.34	2.47	316
P2	$y = 0.00080x + 0.38320$	0.03	−0.00080	14.86 ± 0.89	5.96	–
P3	$y = -0.00438x + 0.65355$	0.52	0.00438	13.40 ± 0.34	2.53	149
P4	$y = -0.0038x + 0.40481$	0.24	0.00380	18.54 ± 0.77	4.17	106
P5	$y = -0.00686x + 0.35369$	0.95	0.00686	18.65 ± 5.35	28.7	52
P6	$y = -0.00496x + 0.68489$	0.83	0.00496	14.54 ± 0.22	1.49	138
P7	$y = -0.00152x + 0.24996$	0.60	0.00152	20.23 ± 2.48	12.3	165
P8	$y = -0.00351x + 0.44695$	0.85	0.00351	14.04 ± 0.31	2.21	127
P9	$y = -0.00069x + 0.22981$	0.33	0.00069	15.43 ± 0.94	6.08	331
P10	$y = -0.00660x + 1.12439$	0.62	0.00660	15.64 ± 0.84	5.38	170
P11	$y = -0.00034x + 0.21049$	0.22	0.00034	17.01 ± 0.48	2.80	622
P12	$y = -0.00365x + 0.53096$	0.94	0.00365	15.90 ± 0.73	4.61	145
P13	$y = -0.00189x + 0.36564$	0.82	0.00189	15.10 ± 0.52	3.45	193
P14	$y = -0.00010x + 0.32471$	0.53	0.00010	14.35 ± 0.22	1.52	326
P15	$y = -0.00095x + 0.76603$	0.48	0.00095	14.60 ± 0.40	2.71	805

D_c: linear healing value, RSD: relative standard deviation, S_c: shape coefficient, SD: standard deviation, $t_{closure}$: time of wound closure, y = A/P (cm), x = t (days), R^2: linear regression factor.
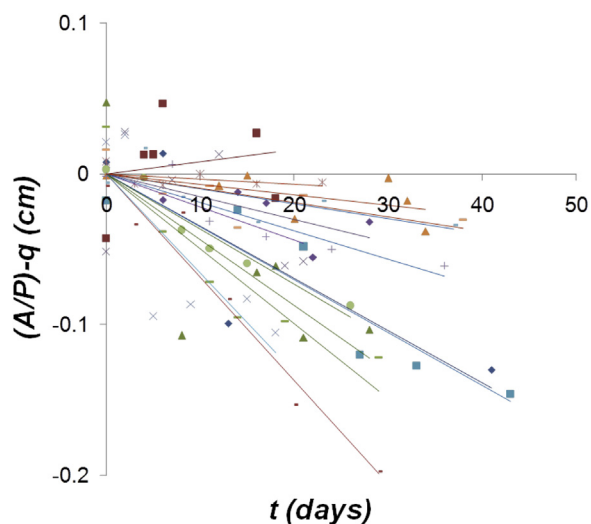
Figure 3 $(A/P) – q$ as a function of time. Data points and linear arrangements for the 15 patients. A: area, P: perimeter, q: intercept of the formula $A/P = -D_c t + q$, where D_c: continuous linear healing rate and t: time (days).

regard, four magnitudes related with initial wound shapes and sizes have been evaluated as follows: initial Area (A^{init}); initial Perimeter (P^{init}); initial Shape coefficient (S_c^{init}) defined as $S_c^{init} = (P^{init})2/A^{init}$, and q. The respective values were plotted in Fig. 4b. A^{init} ranged between 0.78 and 21.1 cm², and no correlation with either D_c ($r = 0.5015$; $p = 0.057$) or D_{avg} ($r = 0.2311$; $p = 0.407$) was found. P^{init} ranged from 3.4 to 17 cm, and respective values correlated with D_c ($r = r -0.5376$; $p = 0.039$), but did not correlate with D_{avg} ($= 0.1687$; $p = 0.548$). A negative correlation was found between S_c^{init} and D_{avg} ($r = -0.6101$; $p = 0.016$), but not between S_c^{init} and D_c ($r = -0.3361$; $p = 0.221$). q values ranged between 0.21 and 1.25 cm, demonstrating no correlation with D_c ($r = -0.353$; $p = 0.197$) or D_{avg} ($r = -0.272$; $p = 0.326$). Thus, taking these results as a whole, we can conclude that there is a weak correlation between the healing rates found by both mathematical methods and the initial wound shape and size.

Wound shape evolution during this study has been documented by the S_c calculation through equation (6). As previously mentioned, S_c is a parameter that does not depend on the size of the analyzed figure, but on its shape. Likewise, a perfect circle has a S_c of 4π, the lowest possible value to be found (Fig. 1). S_c mean values, together with the corresponding SD and RSD, are plotted in Fig. 5a. In this study, S_c values ranged between 13.1 and 18.2, indicating that wounds were not elongated toward any specific direction. There was no correlation ($r = 0.227$; $p = 0.417$) between R^2 values of the linear adjustments (Table 3) from which D_c was calculated and RSD obtained for each patient during wound evolution, indicating that a change in wound shape may not be a cause of loss of linearity. Similarly, no correlation was found between the RSD values from which

D_{avg} was calculated and RSD ($r = -0.231$; $p = 0.408$), indicating that data dispersion for any patient was not necessarily caused by a change in wound shape during the healing process. In fact, small changes in wound shape have been registered, a witnessed by low values of RSD, >6%, with the exception of P5 and P7, for which the corresponding RSD yielded values of 28.7 and 12.3%. Evolution in time of this parameter for these two patients can be observed in Fig. 5b. The wound shape for P5 clearly changed after the first 15 days, adopting a more elongated form during the last 2 weeks (Fig. 5c). Evolution of the wound of P7 appears more erratic, demonstrating S_c values trending up and down, as can be noted in Fig. 5b and c. However, evolution of the wound of P5 exhibited excellent linear behavior in the wound-healing process, with an R^2 value of 0.95 for linear adjustment of data, whereas an R^2 of only 0.60 was obtained for P7. In addition, data for P5 are less dispersed than those for P7 when calculating D_{avg}, demonstrating RSD of 95 and 172%, respectively (Table 1).

We also noted that the patient's health condition reported in Table 1 could not be correlated with D_c or D_{avg}. Furthermore, no statistical differences were found considering Wagner grade (Table 1) and D_c ($U = 17$; $p = 0.463$) or D_{avg} ($U = 21$; $p = 0.841$), employing the Mann–Whitney U test. For this test, the sample corresponding to P6, the only Wagner III patient, has not been considered. Similarly, no differences were found regarding wound type (Table 1) and D_c ($U = 16$; $p = 0.7728$) or D_{avg} ($U = 16$; $p = 0.7728$), utilizing the same statistical test. In fact, only two of the three neuropathic patients showed D_c values > 0.004 cm/day (P8 and P12). The only Wagner III patient (P6) presented a D_c value of 0.00496 cm/day. Wagner I ulcers corresponded to the three neuropathic patients (P8, P12, and P14) plus P9 and P13, and all patients presented D_c values < 0.004 cm/day. The two younger patients (P7 and P10, aged 40 and 45 years, respectively), showed neuroischemic ulcers, with similar D_c values of around 0.006, despite the duration of both of their wounds and that the pathologies differed from each other.

Discussion

The integrated data acquisition technology for the measurement of wound extension, such as photographic systems with adequate software to record and analyze images, and systems that employ stereophotometry, may furnish additional advantages, such as low interobserver variability. In addition, sophisticated systems are able to distinguish by color analysis areas with granulation and necrotic tissue.[18,19] After image treatment, parameters such as A and P may be obtained at different time values. In classical, simple analyses, affordable by nurses and physicians at hospitals and family health centers, healing rates are obtained by calculation of absolute and relative surface
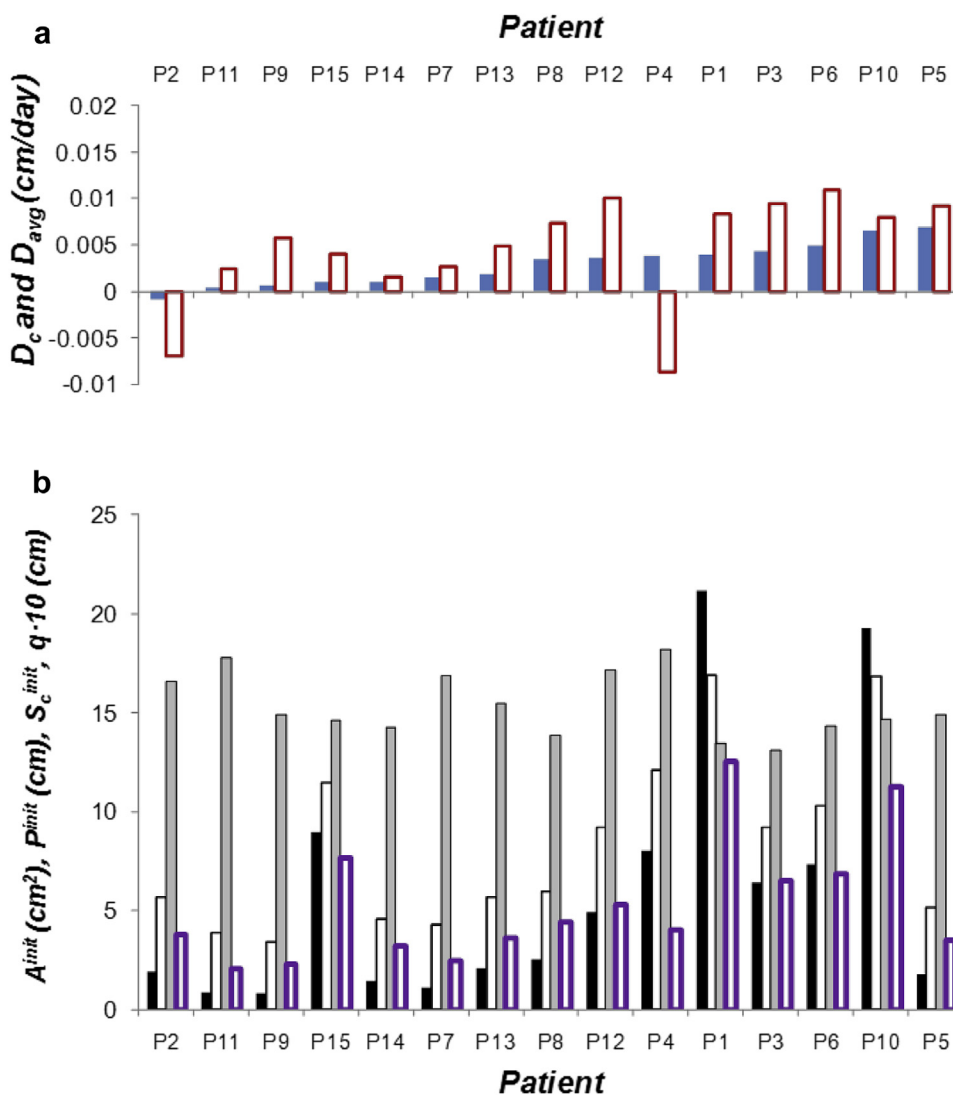
Figure 4 a) D_c (■) and D_{avg} (□) for each patient; b) A^{init} (■), S_c^{init} (□), q values (■), and P^{init} (■) for each patient. A^{init}: initial area, D_{avg}: average linear healing value, D_c: continuous linear healing rate, P^{init}: initial perimeter, q: intercept of the formula $A/P = -D_c t + q$, where D_c: continuous linear healing rate and t: time (days), S_c^{init}: initial shape coefficient.

changes in time and calculation of parameter D.[17] However, these analyses may fail due to large variations in D values obtained between two consecutive clinic visits. Thus, as what has been shown in this study, the high data dispersion achieved when calculating D_{avg} would not allow extracting useful information for decision-making with respect to changing treatment, for example, or for applying any specific product. In our approach, considering the ease of data acquisition, planimetry of the wounds on acetate sheets represents a simple and short time-saving strategy (Fig. 6).[20,21]

The alternative data treatment developed here permits the extraction of hidden information, based on the assumption implicit in the definition of linear healing, i.e., a regular advance of the wound contour toward the wound open area and perpendicular to the wound margin, so that data corresponding to this magnitude are theoretically linked with each other by a linear trend over time. Thus,

the slope of the linear trend, which we denominate D_c, arises from the introduced mathematical model to characterize wound-healing. In addition, the D_c parameter possesses an advantage over D_{avg} that allows for the use of a lower number of values for the analyses, in that the data are linked by a mathematical formula. Also, it provides better visual information because the parameter is represented by the slopes of straight lines in a graph where the wound evolution for different patients can be compared. In order to better understand these terms, the data obtained for P5 are presented in Fig. 7.

In treating data according to the classical method, therefore calculating D_{avg} by means of equation (1), the differences in A and P between two consecutive visits, independent from differences between two other consecutive visits, must be considered. Moreover, individual D values are classically calculated only by treating the data, but
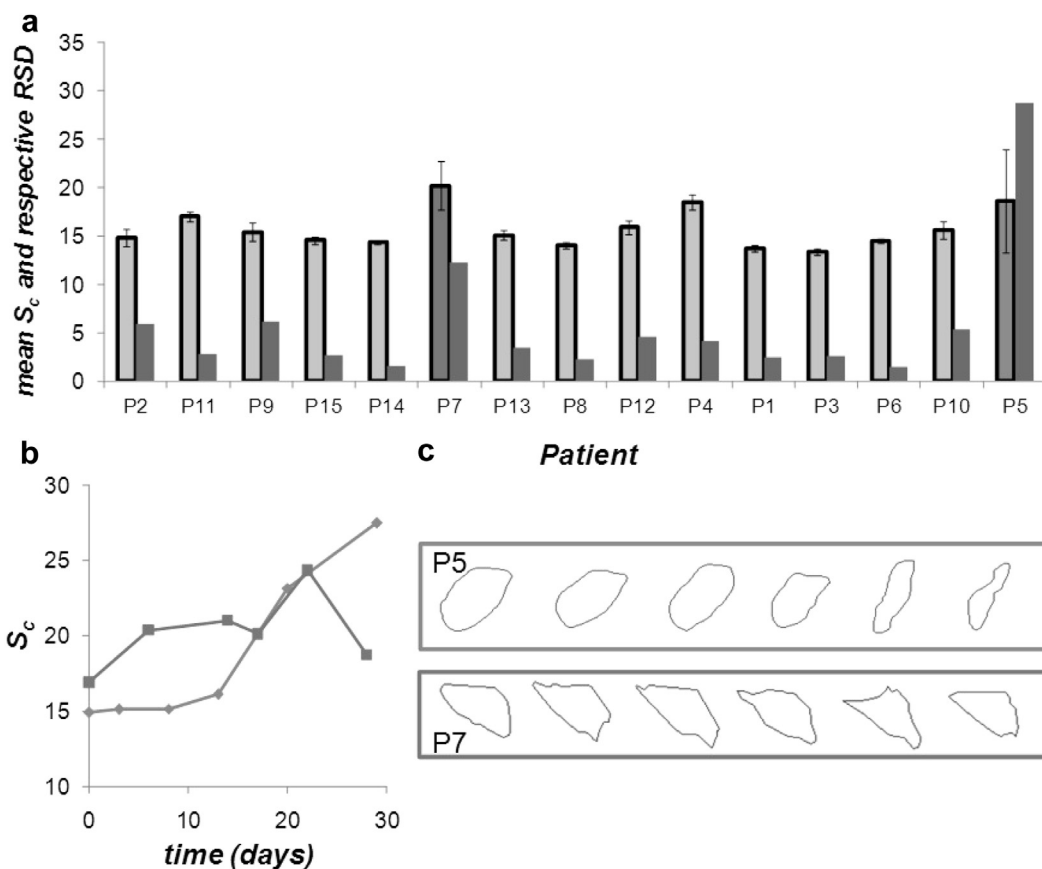
Figure 5   a) Mean S_c (□) (with SD) and respective *RSD* (■) for each patient; b) S_c values for P5 (◆) and P7 (■); c) Wound margins for P5 and P7 (out of scale). P (number): number of the patient, *RSD*: relative standard deviation, S_c: shape coefficient, *SD*: standard deviation.

not graphically. We represent the *A/P* data vs. *t* in Fig. 7 (top left and right). The individual *D* values obtained between each pair consecutive visits are represented by the

slopes of the small segments (Fig. 7, top left). The lines do not completely adjust to the segments linking two consecutive data, in that equation (1) employs P_{avg} instead
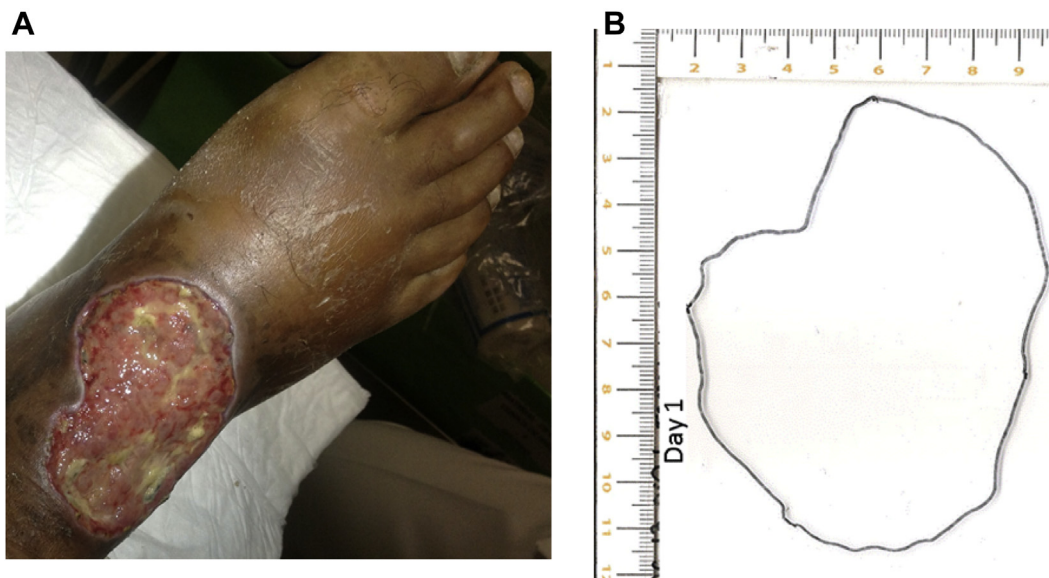
Figure 6   A) Photograph and B) its scanned image of one case of foot ulcer.
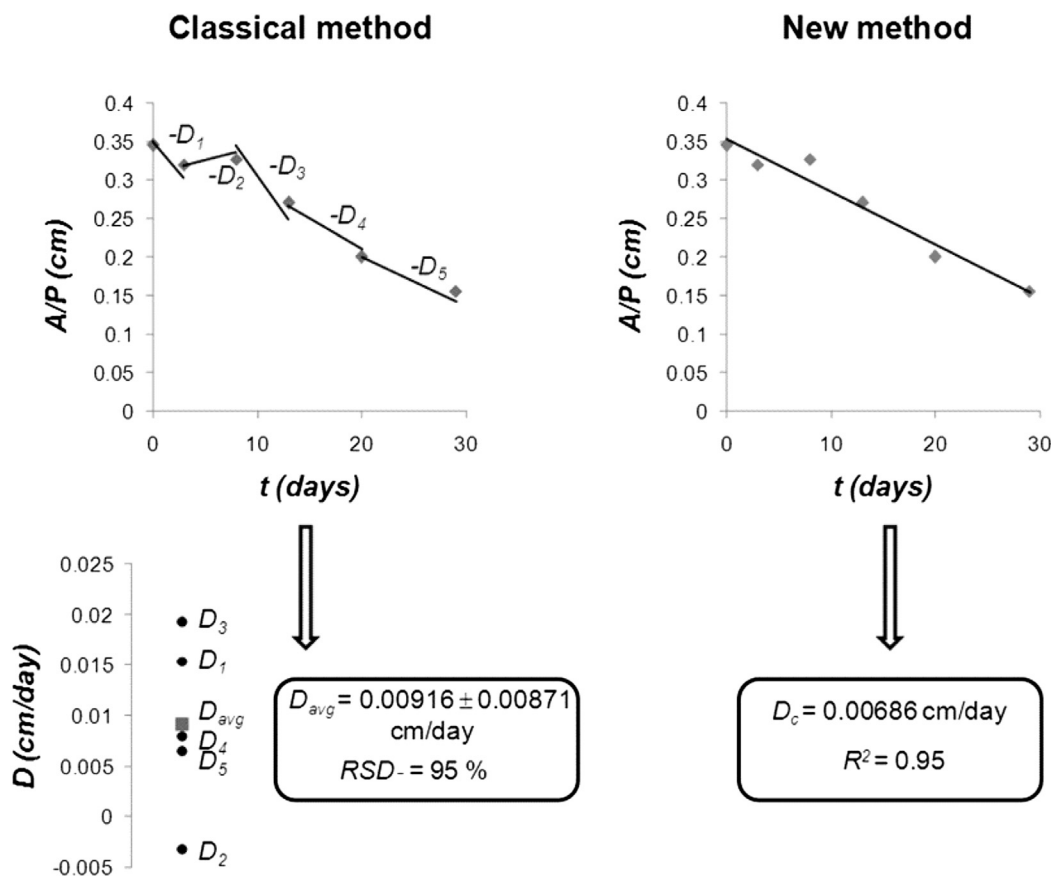
Figure 7   Top left: Data points obtained for P5 (◆), and its treatment according to equation (1); individual D values are graphically shown as the slope of the lines. Bottom left: individual D values are plotted (●), together with the corresponding D_{avg} (■) and its RSD. Top right: Data points obtained for P5 (◆), and their linear adjustment according to equation (5). Bottom right: the D_c value and the corresponding R^2 obtained are shown. A: area, D: linear healing rate, D_{avg}: average linear healing value, P: perimeter, R^2: linear regression factor, RSD: relative standard deviation.

of P. Then, a large dispersion in D values is found, since the trending up and down of the data produces large differences in the slope of the corresponding segments; thus, RSD values are also found to be large (Fig. 7, top and bottom left).

Expression (5) has the advantage over expression (1) in that fewer data points are needed to trace the healing profile, because of the theoretical linear trend; therefore, linkage between data, is considered. Thus, from the mathematical point of view, five visits taken once a week where data are acquired should be sufficient to find the linear trend of the wound-healing by fitting five experimental points. The innovative method presented reflects that the data are not independent one from the other, but are linked by a linear trend. Thus, D_c can be easily calculated, with few data, by obtaining the slope of this linear trend after linear adjustment, with R^2 as the parameter for evaluating the strength of the linear association among the variables. Note that, for P5, the data followed a linear trend with an excellent R^2 of 0.95, which confirmed the good quality of the D_c estimation (Fig. 7, right), whereas an RSD of 95% was obtained for the D_{avg} calculation.

Among information obtained by introducing data on the mathematical algorithm, is the $t_{closure}$, a parameter that could be easily taken into consideration to make a clinical decision. For example, it has been reported, for diabetic foot ulcers that, linearity of the healing process may be lost for ulcers healing beyond 28 days.[17,22] In this regard, $t_{closure}$ should be interpreted as an extrapolation of linear healing during the first 28–35 days of healing, and used for a decision to change treatment rather than as a predictive value. In addition, the correlation found between the values of D_c and R^2 may supply another criterion for decision-making. Low D_c values with low R^2 may indicate poor quality of wound-healing progression. On the contrary, high D_c values with high R^2 may indicate that the treatment is effective. For example, if D_c values > 0.003 cm/day and R^2 > 0.8 are imposed as quality criteria (to this point, arbitrarily), 5 patients (P1, P5, P6, P8, and P12) comply with this requisite. Moreover, these parameters offer means of comparison of the wound evolution of a specific patient before and after changing the treatment, once the latter is decided upon by the medical personnel.

In clinical setting, mathematical formulas based on the argument that the dimension under assessment conforms to a linear phenomenon[23] have been used not only to evaluate wound-healing[24] but also scar evolution.[25]

The data obtained from this small sample of patients suggest that we can predict the type of response to the healing strategy after 4–6 weeks of follow-up. If this is corroborated with a larger study, the possibilities to replicate the prediction of this new formula in other diseases are high, more if we add the use of complex image studies like axial computed tomography (ACT) or Magnetic Resonance Image (MRI).

Data accumulation will aid in establishing quantitative criteria for making a diagnosis of the quality of wound progression and for obtaining more accurate parameters and criteria for comparison of the wound-healing evolution for different patients. The incorporation in the future of more technological tools for image capture, processing, and analysis in clinical practice may be slow, but probably unavoidable. It has been reported in the literature that, providing standard care, the time course of wound-healing in diabetic foot ulcers is predominantly determined by etiologic factors, and to a lesser degree by wound size.[26] However, both the patient's health condition and the wound shape have been invoked to explain differences in healing rates.[14,15,17] In this study, null or weak correlations have been found between D_c or D_{avg} in terms of wound size and shape, parameterized by means of A, P, and S_c, or with the patient's condition.

A clear limitation of the study is the low number of patients. In spite of this drawback, this was a pilot study and the advantages provided by the calculation of D_c and related parameters may represent an important feature for the medical management of several wound types, because accurate results may be easily obtained solely by introducing a few data in a simple algorithm (that may easily be developed in conventional computer-program spreadsheets), appropriate for their use by medical personnel. Interpreting graphic results and quantitative outputs may aid in decision-making process in order to find the most effective treatment for every patient.

Acknowledgments

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