Maggot versus conservative debridement therapy for the treatment of pressure ulcers

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To define the efficacy and safety of maggot therapy, a cohort of 103 inpatients with 145 pressure ulcers was evaluated. Sixty-one ulcers in 50 patients received maggot therapy at some point during their monitored course; 84 ulcers in 70 patients did not. Debridement and wound healing could be quantified for 43 maggot-treated wounds and 49 conventionally treated wounds. Eighty percent of maggot-treated wounds were completely debrided, while only 48% of wounds were completely debrided with conventional therapy alone ($p = 0.021$). Within 3 weeks, maggot-treated wounds contained one-third the necrotic tissue ($p = 0.05$) and twice the granulation tissue ($p < 0.001$), compared to non-maggot-treated wounds. Of the 31 measurable maggot-treated wounds monitored initially during conventional therapy, necrotic tissue decreased 0.2 cm^2 per week during conventional therapy, while total wound area increased 1.2 cm^2 per week. During maggot therapy, necrotic tissue decreased 0.8 cm^2 per week ($p = 0.003$) and total wound surface area decreased 1.2 cm^2 per week ($p = 0.001$). Maggot therapy was more effective and efficient in debriding chronic pressure ulcers than were the conventional treatments prescribed. Patients readily accepted maggot therapy, and adverse events were uncommon. **(WOUND REP REG 2002;10:208–214)**

Pressure ulcers remain a common complication of motor, sensory, or cognitive impairment and they are associated with significant morbidity and costs. Pressure ulcer incidence in acute hospitals is reported to be as high as 38%, and the incidence in extended care facilities can approach 24%.[1] Pressure ulcers increase the duration and costs of hospitalization[2] and can put patients at a four- to sixfold increased risk of death.[3] Despite the many developments in wound care during the past 2 decades, there has been no significant decrease in pressure ulcer prevalence nor any demonstrable improvement in overall outcomes. New treatment paradigms must be examined as we strive to reduce pressure ulcer morbidity.

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ISSN: 1067-1927 $15.00 + 0

MDT	Maggot debridement therapy

For 70 years,[4] maggot therapy (known also as maggot debridement therapy [MDT],[5] or biodebridement)[6,7] has been recognized as an effective method of debridement and wound healing. Medicinal maggots secrete digestive enzymes which selectively dissolve necrotic tissue,[8] disinfect the wound,[9–11] and stimulate wound healing.[12–14] During the 1930s, thousands of clinicians routinely used MDT for treating bone and soft-tissue infections,[15] but by the 1960s, maggot therapy was used only as salvage therapy for a few serious wounds.[16–18]

To assess the utility of MDT for treating pressure ulcers, a small prospective comparative study was initiated at our institution in 1990.[19] Maggot therapy was also provided to patients who did not meet the strict study requirements, or who chose not to participate in the nonblinded study. In order to evaluate the efficacy and safety of maggot therapy objectively and comprehensively, we have now analyzed the outcomes of the entire cohort of pressure ulcer patients who were followed by our service, whether or not they received maggot treatments.

MATERIALS AND METHODS

Between 1990 and 1995, patients with nonhealing wounds were referred to the maggot therapy team for evaluation. Patients found to be appropriate candidates for maggot therapy were followed in-hospital. Noncandidates—those with underlying osteomyelitis or rapidly advancing infection in need of urgent surgical resection—were directed elsewhere, usually for amputation. After obtaining informed consent, wounds were evaluated visually and photographically every week, and wound margins were traced on transparent acetate sheets. Whenever possible, patients were monitored for at least 2 weeks while continuing to receive the treatments prescribed by their primary care provider or the hospital's wound care team ("conventional therapy"). If the wound did not improve, and if the patient and primary care team consented to treatment, then maggot therapy was initiated. This study was conducted with Institutional Review Board approval.

MDT protocol

Maggot therapy was administered by applying disinfected fly larvae (*Phaenicia sericata*) to the wound at a density of five to eight per cm^2. The skin surrounding the ulcer was covered with a hydrocolloid pad (Duoderm, Convatec, Princeton, NJ) out of which was cut a hole to match the ulcer dimensions. This ring of hydrocolloid prevented the maggots from crawling on the intact skin surrounding the wound, and prevented the necrotic wound drainage from coming in direct contact with the skin. It also provided a foundation to which the maggot dressings could be affixed securely. A porous sheet of Dacron® chiffon or a nylon stocking was glued to the hydrocolloid ring such that it covered the wound, creating a "cage" with the maggots inside.[20,21] This cage-like dressing was then topped with a light gauze pad to absorb the necrotic drainage. The top layer of gauze was replaced every 4 to 8 hours because it was quickly soiled by the profuse wound drainage, but the cage-dressing and maggots remained over the wound for cycles of about 48 hours. Two 48-hour cycles were applied each week; saline- or 0.125% sodium hypochlorite-moistened gauze dressings were applied during the 1 to 4 days between MDT cycles.

Patient selection

Our service followed 103 patients with pressure ulcers. The entire cohort was reviewed for the occurrence of adverse events. Quantification of debridement and wound healing was evaluated for the first two ulcers per patient, where those ulcers could be measured reliably from photographs or tracings. Specifically, wounds with complex nonplanar topography, wounds photographed without scale markers, and wounds followed for less than 2 weeks were necessarily omitted from this analysis. A total of 92 wounds in 67 patients met the criteria for analysis of debridement and wound healing efficacy. All wounds that received maggots were considered as "maggot-treated," even when the maggots died in the dressings or were removed accidentally by the nursing staff.

Wound evaluations

Ulcer length, width, circumference, and surface area were calculated from digitized wound images and tracings, using the Image Analyst software package (Automatrix, Inc., Billerica, MA) or Mocha (Jandell Scientific, San Rafael, CA). Patient and wound histories were collected directly from patients or their medical records. Primary outcome measures included changes in relative and absolute surface area, necrotic tissue, and granulation tissue over time. Additional end points included the occurrence of complete debridement and complete wound closure. The wound healing rate, based on studies by Gilman[22] and Margolis et al.,[23] was defined as the change in surface area divided by the mean circumference over time:

$$\frac{\Delta\ \mathrm{SA}_{(t_{2-1})}}{\text{mean circumference}\,(t_{2-1})} \div (t_{2-1}) =$$

$$\frac{(\text{surface area at time } t_2) - (\text{surface area at time } t_1)}{[(\text{circumference at time } t_1) + (\text{circumference at time } t_2)]/2} \div t_{2-1}$$

where t_1 = initial time of observation; t_2 = final time of observation; and t_{2-1} = the period of observation ($t_2 - t_1$), in weeks. Wound healing rates were calculated for $t_{2-1} = 4$ weeks, $t_{2-1} = 8$ weeks, and t_{2-1} = duration of treatment.

Statistical analysis

Normally distributed ordinal and interval data were analyzed using the Student's *t*-test or logistic regression when variance was equal, and Welch's *t*-test when variance was not equal. Ordinal and interval data not normally distributed were evaluated using the Mann–Whitney *U*-test. Nominal data were analyzed using Pearson's chi-square test. Changes in tissue quality and surface area over time were evaluated using repeated measures analysis of variance (ANOVA). Paired *t*-tests were used to compare pre-MDT outcomes with MDT-associated outcomes in the same patients. The hypothesis of equality of means was discarded when the probability (p) of a type I error was $\leq 5\%$. Analyses were performed with SPSS statistical software (SPSS, Inc., Chicago, Illinois).

RESULTS

Between 1990 and 1995, our service followed 103 patients with 145 pressure ulcers. Sixty-one ulcers in 50 patients received maggot therapy at some point during their monitored course (see Figure 1); 84 ulcers in 70 patients did not receive maggot therapy. Seventeen patients had one pressure ulcer treated with MDT and a second ulcer not treated with MDT. Two additional patients received only conventional therapy for their pressure ulcer while receiving MDT for a wound other than a pressure ulcer. Thus, 51 patients in this cohort did not receive maggot therapy for any wound. MDT was not administered to these patients for the following reasons: the patients' doctors did not consent to maggot therapy (11 patients); the wounds improved during the baseline observation period on conventional therapy alone (8); the patients (2) or their decision-making surrogates (2) did not consent to therapy. Twenty-four patients were being followed in anticipation of administering maggot therapy, but they were discharged, died, or were lost to follow-up before they could be treated. (Limited resources prevented us from treating more than four or five patients with MDT at any one time, and the maggot therapy program was terminated in 1996 with many patients still awaiting therapy.) No reason was documented for four patients.

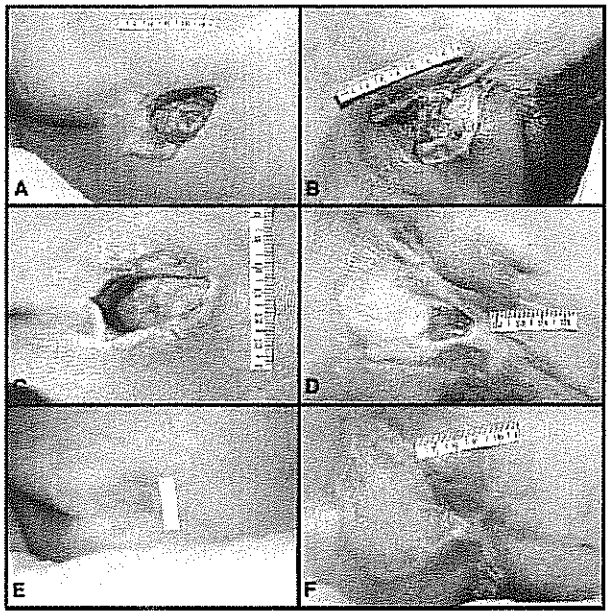

FIGURE 1. Two pressure ulcers treated with MDT. (A) A stage 3 necrotic and undermined sacral ulcer is seen prior to MDT, and (B) 4 weeks later, after maggot therapy. Note that the base is filling with granulation tissue. (C) The wound closed within 9 months with minimal scarring. (D) A 67-year-old spinal cord injured man failed to respond to conventional treatment of his left ischial pressure ulcer. (E) His wound responded to MDT, seen here on day 8, and (F) completely healed on day 18.

All 103 subjects were evaluated for the occurrence of adverse events. Two of the 50 maggot-treated patients complained of pain during MDT; both had previously complained of pain during conventional treatments as well. Maggot-related anxiety was described by one patient treated with MDT and by one patient who declined maggot therapy. None of the seven recorded deaths occurred in patients receiving maggot therapy.

Analysis of debridement and wound healing efficacy was carried out for the 92 wounds in 67 patients that met the analysis criteria. Forty-nine wounds were treated only by conventional therapy; 43 wounds received maggot therapy. Ulcers were almost 60% larger in the maggot-treated group ($p = 0.035$). Also, maggot-treated patients were more often diabetic and spinal cord injured, with a higher average serum albumin. Otherwise, there were no significant differences between the two treatment groups (see Table 1).

Debridement and wound healing differences between those patients treated with or without maggot therapy are detailed in Table 2. Conventional treatments were consistent with the standard of wound care at our facility, and included topical antimicrobial therapy (35%); acemannan and hydrogels (10%); chemical debriding agents (8%); saline-moistened or "wet-to-dry" dressings (8%); hydrocolloids and calcium alginates (6%); growth factors (4%); and multiple combinations of nonsurgical treatments (12%). Almost 17% of the conventionally treated group received bedside or intraoperative surgical debridement.

Maggot-treated wounds were debrided more quickly and completely than were conventionally treated wounds (see also Figure 2). Eighty percent of maggot-treated wounds were completely debrided in less than 5 weeks, while most (52%) non-maggot-treated wounds were still not completely debrided after 5.5 weeks of therapy ($p = 0.021$). Twice as many maggot-treated wounds decreased in size during therapy (84% vs. 37%, $p < 0.001$). Debridement efficacy was further evaluated using repeated measures analysis of variance, with necrotic tissue surface area as the within-subjects factor. The sphericity assumption was not met, so the Huyn-Feldt correction was applied. Analysis of variance indicated no significant change in necrotic tissue for the conventionally treated wounds. Maggot treated wounds, however, were associated with a significant decrease in necrotic tissue ($F\ [1.5, 49.1] = 15.02$, $p < 0.001$), with an average decrease of 3.7 cm^2 necrotic tissue within the first 2 weeks ($p < 0.001$).

Maggot therapy was also associated with rapid growth of granulation tissue and rapid conversion of necrotic and static ulcers to a healthy wound bed which could

Table 1. Characteristics of 92 pressure ulcers in 67 patients treated with or without MDT

	Conventional therapy	MDT
Number of wounds analyzed	49	43
Wound Age, in weeks (range)	34 (4–208)	37 (5–207)
Wound characteristics		
Surface area (cm^2)*	14.0 (9.7–18.2)	22.1 (15.7–28.4)
Necrotic tissue, as a percent of total surface area	34% (23–45)	31% (21–41)
Granulation tissue, as a percent of total surface area	31% (19–42)	27% (16–38)
Depth		
Subcutaneous (Stage 3, superficial)	28 (57%)	14 (33%)
Intramuscular (Stage 3, deep)	17 (35%)	11 (25%)
Down to bone, involving periosteum	4 (8%)	15 (35%)
Into bone, with osteomyelitis	0	3 (7%)
Anatomic location		
Foot and ankle	10 (21%)	11 (25%)
Leg, knee, thigh	3 (6%)	5 (12%)
Sacrum, ischium, trochanter	34 (69%)	25 (58%)
Other	2 (4%)	2 (5%)
Patient age in years (range)	66 (32–91)	62 (26–85)
Underlying medical conditions		
Spinal cord injury; paraplegia*	19%	44%
Diabetes*	17%	37%
Peripheral venous or arterial disease	15%	24%
Cerebral vascular accident	32%	24%
Incontinence of bowel and/or bladder	87%	83%
Cigarette smoker	26%	29%
% ideal body weight (range)	90% (50–162)	101% (65–179)
Albumin (g/dl)*	2.9	3.3
Hemoglobin (g/dl)	11.0	11.1

Unless otherwise noted, 95% confidence intervals are listed parenthetically. Asterisks (*) indicate characteristics that are not evenly distributed between the conventional therapy group and the MDT group ($p < 0.05$).

Table 2. Results of therapy in 92 pressure ulcers treated with conventional therapy or MDT

	Conventional therapy	MDT
n	49	43
Average duration of therapy (weeks)	5.5 (4.9–6.2)	4.8 (4.1–5.5)
Debridement		
Initial necrotic tissue, as a % of total area	34% (23–45)	31% (21–41)
Initial surface area of necrotic tissue, in cm^2	5.95 (3.6–8.3)	6.12 (3.7–8.0)
* Percentage of necrotic wounds completely debrided	48% (26–70)	80% (65–95)
* Weeks until half the necrotic tissue was debrided	4.0 (2.6–5.4)	1.4 (1–1.7)
* Weeks until total debridement of necrotic wounds	17 (7–28)	8 (6–10)
* Change in necrotic surface area (cm^2) per week	+0.3 (−0.9–1.6)	−1.6 (−2.6 to −0.6)
Quality of wound base: preparation for graft or surgical closure		
Initial granulation tissue as % of total area	31% (19–42)	27% (16–38)
Granulation tissue at 4 weeks*	29% (18–40)	69% (56–82)
Percentage of wounds that attained at least 50% granulation tissue*	18 (7–29)	51 (36–66)
Weeks until granulation tissue reaches > 50%	4.7 (2.1–7.3)	2.1 (1.7–2.6)
Change in % granulation tissue per week*	+3.3% (0.9–5.7)	+13% (7–19)
Wound size & and healing		
Initial surface area in cm^2*	14.0 (9.7–18.2)	22.1 (15.7–28.4)
Change in surface area during treatment (cm^2)*	+6.3 (2.5–10.1)	−7.3 (−10.4 to −4.2)
Change in surface area per week*	+1.4 (0.5–2.3)	−1.5 (−2.3 to −0.7)
Percentage of wounds which decreased in surface area within 4 weeks*	44% (27–61)	79% (63–94)
Healing rate at 4 weeks*	−0.038 (−0.847 to −0.008)	0.101 (0.061–0.141)
Healing rate at 8 weeks*	−0.027 (−0.074–0.021)	0.096 (0.057–0.135)
Percentage of wounds that completely healed	21%	39%
Average time until wounds completely healed	13.4 wks (8–19)	12.0 wks (7–17)

Unless otherwise noted, 95% confidence intervals are listed parenthetically. Asterisks (*) indicate characteristics that are not evenly distributed between the conventional therapy group and the MDT group ($p < 0.05$).

appropriately be grafted or surgically closed. The average maggot-treated wound was not only debrided, but covered 60% by healthy granulation tissue within 3 weeks (Figure 3). Twice as many maggot-treated wounds were over 50% covered by healthy granulation tissue during the course of treatment (49% vs. 18%, $p = 0.002$). Analysis of variance (with granulation tissue as the within-subjects factor) indicated no significant change in granulation tissue for the

MDT appears to be a valuable modality for treating nonhealing pressure ulcers. The overall efficacy of conventional therapy was not assessed in this study because this study examined only those wounds that appeared not to be responding to conventional care. In this setting, MDT proved to be more effective than was another course of conservative wound therapy. Most of the conventionally treated wounds received conservative, nonsurgical care, so it is impossible to compare the efficacy of MDT to that of surgical debridement. Surgical debridement is likely to be more efficient than maggot debridement, but the ultimate impact of each on wound closure can be evaluated only in a prospective comparative trial. In situations where surgery is not feasible, MDT appears to be superior to the most commonly used nonsurgical alternatives.

The mechanisms underlying maggot-induced wound healing are not known, but it may be that the maggots consume or inactivate inhibitory proteases and cytokines. Maggot-secreted cytokines[24] and growth factors[25] also may play a role.

Maggot therapy was well accepted by patients. The most common adverse event was discomfort, reported by 4% of maggot-treated patients. This complaint never prompted any patient to discontinue maggot therapy. These observations are consistent with the fact that maggot therapy is occasionally used in patients who are intolerant to surgical debridement pain or anesthesia, even though maggot therapy itself may be accompanied by discomfort.

Maggot-related anxiety was not as common as had been described in the 1930s,[15] occurring in only one of our MDT patients and one patient who declined maggot therapy. Perhaps we rarely encountered anxiety because our study population of war veterans was not easily perturbed by insects or perhaps our study population was not comfortable professing such anxiety, whether or not it existed.

With 95% of patients consenting to treatment when asked, maggot therapy was clearly better accepted by patients than it was by the medical and administrative staff, who frequently dissuaded or disallowed their patients to receive maggot therapy, whether or not the patient consented to treatment. The nursing staff also reacted in ways that were not anticipated. For example, some senior nursing staff assigned maggot-treated patients to new and temporary staff without identifying the patients' unique dressing needs. Allowing these uninitiated nurses to inappropriately remove maggot-filled dressings before reading the patients' treatment orders proved to be a powerful and perhaps well-deserved lesson for those nurses who did not first read orders; but it was a very frustrating experience for the patients and the maggot therapy staff who had to replace or discontinue the maggot dressings. Application of "*do not remove this dressing*" labels directly on the maggot dressings reduced the occurrence of these incidents.

The scientific weakness of any retrospective study is the possibility that the bias that accompanies a nonrandomized selection may influence the outcome. This study was designed to minimize this bias as much as possible. While not random, the assignment of treatment groups generally fell outside the control of the study team. Wounds that responded well to conventional therapy were not treated with maggot therapy. For wounds failing conventional therapy, the decision to treat with maggot therapy was made by the patient. Our analysis of pre-MDT conventional therapy showed that the wounds subsequently treated with maggot therapy indeed were failing to respond to conventional therapy. The maggot-treated wounds were larger and more recalcitrant to treatment. Thus, there appears to have been no selection bias in favor of maggot therapy. The difference in nutritional status (higher albumin level in the maggot-treated patients) potentially benefits the maggot therapy group. This inequity probably reflects the fact that the younger and more alert patients, still active in directing their own medical care, tended to request maggot therapy more commonly and forcefully than did the patients with dementia and stroke and their conservators.

This investigation provides the most objective analysis of maggot therapy to date. Only two other comparative studies have been published, both prospective but with fewer than 10 patients per treatment arm.[19,26] Neither of these prior studies examined wound closure as an end point. More than 1000 physicians and surgeons are now using MDT as a treatment option in wound care,[27] yet most of the published reports continue to be anecdotal,[28–34] and the optimal role for maggot therapy remains undefined.

Prospective clinical trials of maggot therapy are now warranted. Clinical trials should compare maggot therapy to conservative medical treatments, and to surgical debridement with or without vacuum-assisted closure. Clinical trials are needed to determine the value of maggot therapy for treating not only pressure ulcers, but also venous stasis ulcers, diabetic foot ulcers, burns, and postsurgical wounds. In addition to efficacy and safety, future studies must address the optimal frequency and duration of maggot treatment cycles, the cost-effectiveness of MDT, and conditions in which maggot therapy is likely to be futile (for example, at what measurable level of hypoperfusion is an extremity wound unlikely to respond to maggot therapy).

ACKNOWLEDGMENTS

Toni Espinoza Ferrel, MPH, provided critical statistical assistance. Many individuals contributed to patient care, wound assessment, data entry, chart reviews, or adminis-

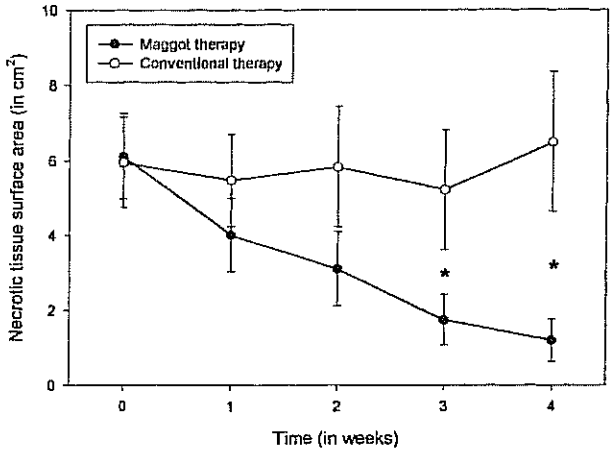

FIGURE 2. Average surface area (cm^2) of necrotic tissue for wounds treated with MDT ($N = 43$) or conventional therapy only ($N = 49$). Error bars indicate standard error; asterisks indicate significant differences in mean surface area ($p < 0.05$).

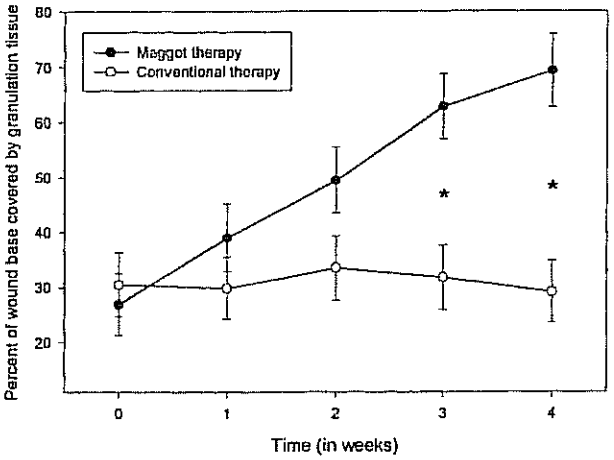

FIGURE 3. Average percentage of wound base covered by granulation tissue during MDT ($N = 43$) or conventional therapy only ($N = 49$). Error bars indicate standard error; asterisks indicate significant differences in mean percentage of granulation tissue ($p < 0.05$).

conventionally treated wounds. Maggot treated wounds, however, were associated with a rapid spread of granulation tissue ($F\ [1.89, 56.6] = 25.5$, $p < 0.001$), where 25% of the wound surface was covered by new granulation tissue within the first 2 weeks of therapy ($p < 0.001$). Nearly twice as many maggot-treated wounds ultimately healed (39% vs. 21%), most within 12 weeks; but this difference failed to reach statistical significance as defined in this study ($p = 0.058$).

No single factor was associated with successful debridement except treatment with maggot therapy (Pearson's chi-square [8.380; 1], $p = 0.004$). Among the maggot-treated patients, failure to achieve adequate debridement (that is, failure of MDT to debride at least 95% of the wound base) was not associated with wound size, patient age, nutritional status, diabetes, or cigarette smoking.

Thirty-one maggot-treated wounds were first followed for 2 to 8 weeks (average: 4.8 weeks) while still receiving conventional therapy. They were then treated for 2 to 8 weeks more (average: 5.2 weeks) with maggot therapy. Paired *t*-test analyses revealed that these wounds progressed in size from 18.0 cm^2 (95% CI, 11.4–24.5) to 24.1 cm^2 (95% CI, 16.3–31.9) during conventional therapy (an increase of 1.2 cm^2 per week), then decreased in size during MDT, from an average of 24.7 cm^2 (95% CI, 16.7–32.6) to 18.1 cm^2 (95% CI, 12.1–24.2), representing a decrease in surface area of 1.2 cm^2 per week ($p = 0.001$). The amount of necrotic tissue at the beginning of conventional and maggot therapy was equal (5.6 cm^2 and 5.4 cm^2, respectively); but by the end of therapy, conventional therapy had debrided very little necrotic tissue (1.0 cm^2) compared to MDT (4.2 cm^2 necrotic tissue debrided; $p = 0.003$).

Patient willingness to undergo maggot therapy was assessed by evaluating consent data. All of the 50 patients treated with MDT gave written consent. Of the 53 patients in this cohort who received no maggot therapy, 19 gave written or verbal consent, 4 declined therapy, and 30 were not asked. Thus, only 4 (5%) of 73 patients or their conservators declined maggot therapy. Twenty of the questioned patients were unable to give informed consent, so consent was solicited from next of kin or the patients' conservators. Two (10%) of these surrogate decision makers did not consent to maggot therapy. In contrast, only 2 (4%) of the 53 patients who were themselves capable of giving informed consent declined therapy.

DISCUSSION

This analysis shows that maggot therapy was more effective and efficient in debriding chronic pressure ulcers than many of the conservative treatments currently prescribed. Maggot-treated wounds were debrided two to four times faster, even though they were initially larger than those wounds not treated with MDT. Maggot-treated wounds were also twice as likely to decrease in size, and twice as likely to develop granulation tissue during the average 5- to 6-week treatment period. It is of note that nearly twice as many maggot-treated wounds completely healed (39% vs. 21%), despite the fact that 16% of the conventionally treated patients were specifically not treated with maggot therapy because they were said to be responding well to conventional therapy; but this difference failed to reach statistical significance ($p = 0.058$).

trative support, including: Julie Sherman; Randall Sullivan, RN; Rodney Wishnow, MD; and Frederic Wyle, MD. This work was supported, in part, by grants from the Spinal Cord Research Foundation of the Paralyzed Veterans of America (1990), the California Paralyzed Veterans of America (1991), and the Andrus Foundation of the American Association of Retired Persons (1992–1995).

REFERENCES

1. National Pressure Ulcer Advisory Panel. Pressure ulcers in America: prevalence, incidence, and implications for the future. An executive summary national pressure ulcer advisory panel monograph. Adv Wound Care 2001;14:208–15.
2. Allman RM, Goode PS, Burst N, Bartolucci AA, Thomas DR. Pressure ulcers, hospital complications, and disease severity: impact on hospital costs and length of stay. Adv Wound Care 1999;12:22–30.
3. Burd C, Langemo D, Olson B, Hanson D, Hunter S, Sauvage T. Skin problems: epidemiology of pressure ulcers in a skilled care facility. J Gerontol Nursing 1992;18:29–39.
4. Baer W. Sacro-iliac joint—Arthritis deformans—viable antiseptic in chronic osteomyelitis. Proc Int Assem Inter-State Postgrad Med Assoc N Am 1929;371:365–72.
5. Sherman RA, Wyle FA, Vulpe M, Wishnow R, Iturrino J, Watson M, Martin G. Maggot therapy for treating pressure sores in spinal cord patients. J Am Paraplegia Soc 1991;14:200. [Abstract]
6. Kennedy KL, Tritch DL. Debridement. In: Krasner D, Kane D. editors. Chronic wound care. 2nd ed. Wayne, PA: Health Management Publications, 1997: 227–34.
7. Sherman RA. Maggot therapy in modern medicine. Infect Med 1998;15:651–6.
8. Vistnes LM, Lee R, Ksander GA. Proteolytic activity of blowfly larvae secretions in experimental burns. Surgery 1986;90:835–41.
9. Robinson W, Norwood VH. Destruction of pyogenic bacteria in the alimentary tract of surgical maggots implanted in infected wounds. J Lab Clin Med 1934;19:581–6.
10. Simmons SW. A bactericidal principle in excretions of surgical maggots which destroys important etiological agents of pyogenic infections. J Bacteriol 1935;30:253–67.
11. Pavillard ER, Wright EA. An antibiotic from maggots. Nature 1957;180:916–7.
12. Baer WS. The treatment of chronic osteomyelitis with the maggot (larva of the blow fly). J Bone Joint Surg 1931;13:438–75.
13. Robinson W. The role of surgical maggots in the disinfection of osteomyelitis and other infected wounds. J Bone Joint Surg 1933;15:409–12.
14. Sherman RA, Hall MJR, Thomas S. Medicinal maggots: an ancient remedy for some contemporary afflictions. Annu Rev Entomol 2000;45:55–81.
15. Robinson W. Progress of maggot therapy in the United States and Canada in the treatment of suppurative diseases. Am J Surg 1935;29:67–71.
16. Horn KL, Cobb AH, Gates GA. Maggot therapy for subacute mastoiditis. Arch Otolaryngol 1976;102:377–9.
17. Teich S, Myers RAM. Maggot therapy for severe skin infections. South Med J 1986;79:1153–5.
18. Bunkis J, Gherini S, Walton RL. Maggot therapy revisited. West J Med 1985;142:554–6.
19. Sherman RA, Wyle FA, Vulpe M. Maggot debridement therapy for treating pressure ulcers in spinal cord injury patients. J Spinal Cord Med 1995;18:71–4.
20. Sherman RA, Tran J, Sullivan R. Maggot therapy for treating venous stasis ulcers. Arch Dermatol 1996;132:254–6.
21. Sherman RA. A new dressing design for treating pressure ulcers with maggot therapy. Plast Reconstr Surg 1997;100:451–6.
22. Gilman TH. Parameter for measurement of wound closure. Wounds 1990;3:95–101.
23. Margolis DJ, Gross EA, Wood CR, Lazarus GS. Planimetric rate of healing in venous ulcers of the leg treated with pressure bandage and hydrocolloid dressing. J Am Acad Dermatol 1993;28:418–21.
24. Mumcuoglu KY, Miller J, Ioffe-Uspensky I, Barak V. The potential of maggots to secrete cytokines in vitro. Fifth International Conference on Biotherapy, Wurzburg, Germany, 2000. [Abstract]
25. Prete PE. Growth effects of *Phaenicia sericata* larval extracts on fibroblasts: mechanism for wound healing by maggot therapy. Life Sci 1997;60:505–10.
26. Wayman J, Nirojogi V, Walker A, Sowinski A, Walker MA. The cost effectiveness of larval therapy in venous ulcers. J Tissue Viability 2000;10:91–6.
27. Sherman RA. Maggot therapy: the last five years. Bull Eur Tiss Repair Soc 2000;7:97–8.
28. Óvári A, Farkas R, Adrián E. Experiences in wound treatment with sterile maggots in Hungary. [in Hungarian] Lege Artis Medicinae 1998;8:874–9.
29. Mumcuoglu KY, Ingber A, Stessman J, Friedmann R, Schulman H, Bichucher H, Ioffe-Uspensky I, Miller J, Galun R, Raz I. Maggot therapy for the treatment of diabetic foot ulcers [Letter]. Diabetes Care 1998;21:2030–1.
30. Mumcuoglu KY, Ingber A, Gilead L, Stessman J, Friedmann R, Schulman H, Bichucher H, Ioffe-Uspensky I, Miller J, Galun R, Raz I. Maggot therapy for the treatment of intractable wounds [Letter]. Int J Dermatol 1999;38:623–4.
31. Wollf H, Hansson C. Larval therapy for a leg ulcer with methicillin-resistant *Staphylococcus aureus*. Acta Derm Venereol 1999;79:320–1.
32. Fleischmann W, Russ M, Moch D, Marquardt C. [Biosurgery—maggots, are they really the better surgeons?] Chirurg 1999;70:1340–6.
33. Thomas S, Andrews A, Jones M, Church J. Maggots are useful in treating infected or necrotic wounds. BMJ 1999;318:807–8.
34. Namias N, Varela JE, Varas RP, Quintana O, Ward CG. Biodebridement: a case report of maggot therapy for limb salvage after fourth-degree burns. J Burn Care Rehab 2000;21:254–7.