



Evaluation of the combined use of ultrasound irradiation and wound dressing on pressure ulcers

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Objective: To evaluate the effect of ultrasound when used alongside standard care in the treatment of pressure ulcers; outcome measures were reduction in wound size and exudates weight.

Method: Five patients (two male and three female, age range: 76–92 years) with seven ulcers participated in this study. They had National Pressure Ulcer Advisory Panel (NPUAP) stage III or IV pressure ulcers. We conducted an ABABA study (A: standard treatment with dressings that promote a moist wound healing environment; B: ultrasound irradiation administered to the pressure ulcer through the same dressing used in period A; each period lasted 2–4 weeks). Six ulcers each were randomised to either the treatment group or control group. One ulcer not randomised, but was the first to receive ultrasound in the BABA sequence with a view to determining if the pilot was feasible. The control group received sham ultrasound in period B. Pulsed ultrasound (20% duty cycle, $0.5\text{W}/\text{cm}^2$ on the wound surface, 1MHz or 3MHz, for 10 minutes) was applied five times weekly.

Results: In the treatment group, two ulcers markedly decreased in size after 3–4 weeks of US treatment, one ulcer decreased in size soon after initiation of treatment and one ulcer showed no clear reduction in size. The volume of exudate was greater in period B than A in two ulcers that reduced markedly in size after 3–4 weeks of US treatment. None of the ulcers in the control group decreased markedly in size.

Conclusion: This pilot study suggests that US used alongside standard treatment might promote the healing of pressure ulcers. However, larger studies are required to determine the efficacy and mechanism of US treatment for PUs.

Declaration of interest: None.

Key Words: ultrasound treatment; pressure ulcer; moist wound healing; ultrasound permeability

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Ultrasound (US) promotes the release of cytokine which induces angiogenesis from fibroblasts *in vitro* and formation of granulation tissue *in vivo*.^{1,2} However, there is no evidence that US therapy promotes healing in chronic wounds, including pressure ulcers (PUs).^{3,4}

Selkowitz et al., who reported on their use of US on a single patient with a stage III PU, found that it did not accelerate healing.⁵ Ter Riet et al., who compared US with sham US in a total of 85 patients, found no difference in healing rates and healing speeds between the two treatments.⁶

Selkowitz et al. irradiated only the periphery of the wound, whereas ter Riet et al. irradiated the actual wound surface, to which they first applied an US gel. Irradiating the wound surface is more likely to be effective than just targeting the wound edges as it contains more granulation tissue; however, the effect of the US gel on wound healing has not been evaluated.

Other reports have also found that ultrasound did not accelerate healing, but they did not mention whether there were any materials or objects between the wound surface and the US probe.⁷⁻⁹ In such cases, what is considered to be the optimum dosage might, in fact, be insufficient to penetrate these materials/objects and so effectively irradiate the wound surface.

As a moist environment promotes healing, wounds being treated with US would still need to be covered with a dressing.¹⁰ The permeability of the dressing material would therefore need to be determined. It would also be necessary to determine the US intensity (which is dose dependent) needed to penetrate the dressing and infiltrate the wound surface as this has not been determined.¹¹

This pilot study to investigate the efficacy of US irradiation when used in the treatment of PUs covered with a wound dressing. The outcome measures were reduction in wound size and the extent of exudation.

Granulation tissue has permeable capillaries, in which fluid exhibits no movement other than oscillation.¹² Mitragotri and Kost reported that US stimulation enhances stratum corneum permeability.¹³ It is possible that US can stimulate the capillaries and promote plasma exudation. Indeed, in our clinical practice, we have observed that US treatment is associated with increased exudate production. We therefore included it as an outcome measure.

Method

Inclusion criteria were the presence of National Pressure Ulcer Advisory Panel (NPUAP) stage III or IV PUs. Exclusion criteria were clinical signs of local wound infection, extensive necrotic tissue, diabetes mellitus type 2 and/or peripheral arterial disease. Participants were inpatients who were receiving standard wound care including surgical debridement, topical antimicrobials and pressure redistribution. None had received US therapy before entry into the study.

Ethics committee approval was received for the study. All patients gave written informed consent.

Study protocol

All patients received standard wound care throughout the study. Each PU received standard treatment alone for 2–4 weeks (period A) and standard treatment plus either US or sham US for 2–4 weeks (period B) in an ABABA sequence.

The ulcers were randomly assigned (via a toss of a coin) to the US group or the control group; the latter group received sham US at period B.

Standard wound care

In all cases, we avoided having patients lie or sit in a position that exerted pressure on existing ulcers. In addition, they were repositioned every two or three hours. All beds were fitted with either urethane foam or air pressure-redistributing mattresses (Prime Dx, Molten, Japan). Nutrient intake was by tube feeding or oral intake, and a blood test was carried out

every month to measure levels of albumin, haemoglobin and C-reactive protein.

Standard treatment

All pressure ulcers were covered with a hydrocolloid dressing (Tegasorb or Tegasorb Thin; 3M Health Care, Japan).

To avoid US reflection, a polyurethane film (either OpSite Flexifix, Smith & Nephew, Japan or Perme-roll, Nitto Medical, Japan) was placed over the hydrocolloid dressing; any air bubble between the layers were removed.

Sugimoto et al. have reported that the above dressings are permeable to US.¹¹

The wound and surrounding skin were cleansed with warm water and slightly acidic soap (pH 5.6; Baby Body Soap, Pigeon, Japan) at dressing change.

This standard treatment was conducted by the nurses and investigators.

Ultrasound treatment

The area of dressing in which exudate seeped fully was covered with US gel (Aquasonic, Parker, US); US irradiation was applied with the dressing in place (Fig 1).

The protocol stipulated that a frequency of 1MHz should be used for all ulcers, except those located close to the bone, when 3MHz should be applied instead. A higher frequency of 3MHz will avoid this potential effect.¹⁴

Based on these MHz frequencies and the US permeability of each dressing, we determined that the US intensity needed to be 0.5W/cm² at the wound surface (Fig 2).

Reher et al.¹ reported that the best intensity to promote cytokine release from monocytes, fibroblasts and osteoblasts is 0.1 or 0.4W/cm². Sugimoto et al.² found that granulation is promoted at 0.6W/cm². Intensities of 0.1–0.8W/cm² or 0.5–1.0W/cm² are recommended clinically for chronic wound healing.^{15,16}

Other parameters were common in the US treatment of PUs (20% duty cycle; 10 minutes' treatment time; five sessions per week; beam non-uniformity ratio 3.2 or 3.5; effective radiating area 5.5cm² or 6.0cm²; probe movement speed, about 1cm/second) (Table 2).

The US device used in this study was ItoUS750, which is used in a wide range of medical conditions.

Measurement procedure

To evaluate the effect of the US treatment, wound size and exudate weight were measured at each dressing change. In addition, the DESIGN scale was used to evaluate the total characteristics of each PU.¹⁷

DESIGN is a PU classification tool that is widely used in Japan. The acronym refers to the characteristics that the tool classifies: Depth, Exudate, Size, Infection, Granulation and Necrosis; an extra character, P, is added to the acronym if a pocket (undermining) is present. The severity of each item is classified as 'slight', indicated by lower-case letters, or 'serious', indicated by upper-case letters. In addition, a point system defines the status of each item, with higher scores indicating greater severity and lower scores indicating less severity. Full details were published in Sanada et al.¹⁷

Wound size A pen-tablet system (Intuos 3, Wacom, Japan) was used to measure the wound. A double layer of transparent film was placed over the wound and the wound perimeter was traced with a marker pen on the upper layer. The lower layer was then discarded and the tracing transferred to the tablet using a dedicated pen. This enabled the wound shape to be digitised and the area measured using Scion Image software.

Exudate weight This was measured by subtracting the weight of the dressing before application from the weight

immediately after removal. Measurements were conducted at regular intervals, which varied with each wound.

To exclude the effect of urinary incontinence, we checked the colour of the dressing, which turns white when it absorbs aqueous fluid. Any dressings that did this were excluded from the analysis.

Results

Five patients were recruited into this pilot study. This number was deemed sufficient for a pilot. Patient demographic and wound characteristics are given in [Table 1](#). Two patients had a PU on both lower extremities, giving a total of seven wounds. All of the wounds were free of infection and had little necrotic tissue. None of the patients had diabetes or peripheral arterial disease.

Patients and investigators were unaware of the treatment allocation except in the case of ulcer 1 only, when the investigators knew the treatment allocation (in order to determine whether to proceed with the trial).

One ulcer (ulcer 2) extended down towards the bone and so received 3MHz.

Three patients with four ulcers (ulcers 1–4) were randomised into the US group and two patients with three ulcers (ulcers 5–7) were randomised to the control (sham) group.

DESIGN values decreased in all wounds except ulcer 6. A marked reduction in wound size was observed only in the US group.

There was no correlation between haemoglobin, albumin or CRP values and wound size. Wound closure was observed in ulcer 7.

Ultrasound group

Wound size In ulcers 1 and 2, a marked reduction in wound size was observed after 3–4 weeks of US treatment. In ulcer 3, a reduction was observed as soon as US treatment began. In ulcer 4, no clear reduction was seen.

Exudate weight In ulcers 1 and 2, exudate weight increased during US therapy. In ulcer 3, there was no such increase. In ulcer 4, exudate weight could not be measured as it leaked from the dressing.

Results for individual PUs are given in [Figs 3–6](#). [Fig 7](#) showed a marked reduction in size in ulcer 3.

Control (sham) group

Wound size These ulcers showed no marked reduction in wound size. One ulcer (ulcer 6) was withdrawn from the study after it increased in size.

Exudate weight In ulcers 5–7, exudate weight was dependent on wound size; no increase in weight was recorded.

Results for individual ulcers are given in [Figs 8–10](#).

Discussion

Three of the four ulcers in the US group reduced markedly in size after US treatment. No such reduction was observed in the control group.

Only Selkowitz et al. provided detailed results on the effect of US on PU healing. They found it had no effect on outcomes; however, in this study the treatment period was two weeks and the US was applied to the skin surrounding the wound.⁵

Our results suggest that US irradiation of the wound surface at an intensity of $0.5\text{W}/\text{cm}^2$, when the wound is covered with dressings that promote a moist environment, is effective for wound healing. It is possible that the US promoted

wound contraction, particularly in ulcers 1 and 3, as shown by a significant increase in the speed of ulcer area reduction. The reason for the lack of a clear improvement in ulcer 4 was the pocket and extent of the wound. A longer irradiation time might therefore be required for such ulcers.

There was no reported increase in exudate weight in the control group, as in previous studies¹⁸ Two ulcers (1 and 2) in the US group produced more exudate following treatment. Increased exudate was not seen in ulcer 3, which was also in the US group. Plasma exudation from ulcer 3 might have been inhibited by the relative lack of granulation tissue, when compared with other ulcers.

It has been suggested that excess fluid serves as a physical and chemical deterrent to wound healing.¹⁹ In the case of ulcer 3 only, wound size reduced as soon as US treatment began. Therefore, without excessive exudation, the wound surface may reduce rapidly. It might be necessary to reduce the weekly number of US treatments when excessive exudate is observed.

The small sample size makes it impossible to determine whether US therapy is more effective than standard treatment. Furthermore, the rate of healing in stage III PUs treated with hydrocolloid dressings has not been reported in other studies.^{5,20} Further clinical studies involving more wounds need to be conducted. In addition, plasma proteins and cytokines in the exudate should be measured biochemically.

Conclusion

The efficacy of US in the treatment of PUs is not certain. In the present study, its use, when delivered at an intensity that can penetrate permeable dressings that keep the wound moist, had a positive effect on healing. More studies are required to determine the efficacy and mechanism of US treatment for PUs. We intend to follow up this pilot study with multicentred study. n

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Figure legends

Table 1. Patient characteristics

Table 2. Ultrasound therapy parameters

Fig 1. Procedure for ultrasound irradiation

Fig 2. Attenuation of ultrasound intensity

Fig 3. Wound size and exudate weight versus time for ulcer 1.

During the B1 period, the neoplastic epithelium around the wound was ruptured by the external force, thus, the wound size increased. At the end of the B1 period, the area closed again. The shape and size of the other area of the wound remained unchanged throughout the B1 period (rate of area reduction on black plots during days 1–20: $-0.03\text{cm}^2/\text{day}$). Shortly thereafter, however, wound size reduced markedly (days 20–24: $0.41\text{cm}^2/\text{day}$). Wound size did not then change until the middle of the B2 period (days 24–57: $0.01\text{cm}^2/\text{day}$). As in the B1 period, wound size began to reduce markedly again at the end of the B2 period (days 57–79: $0.11\text{cm}^2/\text{day}$). Overall, a marked reduction in size was identified after three weeks of ultrasound treatment. Exudate weight increased in the B2 period. DESIGN values fell from 8 (d2e2s2i0g2n0) to 5 (d2e1s1i0g1n0) by the end of the study.

Fig 4. Wound size and exudate weight versus time for ulcer 2.

During periods A1 and B1, wound size reduced uniformly ($0.06\text{cm}^2/\text{day}$). Shortly thereafter, however, the rate of size reduction accelerated (days 56–75: $0.10\text{cm}^2/\text{day}$). The wound then stopped reducing in size until after three weeks of treatment, when it began decreasing again. As with ulcer 1, marked size reduction was recognized after three to four weeks of ultrasound treatment. Exudate weight increased in the B1 period. DESIGN values decreased from 8 (D3e2s2i0g1n0) to 4 (d1e1s1i0g1n0) throughout the study.

Fig 5. Wound size and exudate weight versus time for ulcer 3.

During the A1 period, wound size remained unchanged (days 1–15: $0.01\text{cm}^2/\text{day}$), but at the beginning of the B1 period, wound size began to reduce suddenly (days 15–29: $0.09\text{cm}^2/\text{day}$). The wound then continued reducing in size until the end of B2 period, although the rate of size reduction became slower. Exudate weight changed in accordance with wound size, and an increase in the B period was not seen. DESIGN values decreased from 7 (D3e1s1i0g2n0) to 5 (d2e1s1i0g1n0) throughout the study.

Fig 6. Wound size and exudate weight versus time for ulcer 4.

During the A1 period, the wound size increased gradually, but from the B1 period, wound size began to decrease. Then, wound size decreased constantly until the end of the study. DESIGN values decreased from 17 (D4e2s4i0g2N1P4) to 14 (d3e2s4i0g1n0P4) throughout the study.

Fig 7. Change of wound surface on ulcer 3: at end of A1 period (a) and end of B1 period (b).

Fig 8. Wound size and exudate weight versus time for ulcer 5.

Wound size increased or decreased throughout this study, but this change was seen in period A and B. Exudate weight changed in accordance with wound size. DESIGN values decreased from 11 (D4e2s2i0g2N1) to 7 (d2e2s2i0g1n0) throughout the study.

Fig 9. Wound size and exudate weight versus time for ulcer 6.

Wound size and exudate weight increased gradually. DESIGN values increased from 6 (d2e1s2i0g1n0) to 8

(d2e2s3i0g1n0) throughout the study.

Fig 10. Wound size and exudate weight versus time for ulcer 7.

Wound size decreased throughout the study. Exudate weight changed in accordance with wound size. DESIGN values decreased from 7 (d2e2s2i0g1n0) to 0 (d0e0s0i0g0n0) throughout the study.

Table 1

Patient no.	Age	Sex	Underlying disease	Ulcer no.	Location	NPUAP stage	DESIGN value
1	92	Female	Stroke, hypertension	1	Ilium	III	d2e2s2i0g2n0
2	84	Male	Alzheimer-type dementia, chronic hepatitis C	2	Lateral malleolus	III	D3e2s2i0g1n0
				3	Lateral malleolus	III	D3e1s1i0g2n0
3	76	Female	Parkinson disease, hypertension	4	Sacrum	IV	D4e2s4i0g2N1P4
4	77	Male	Alzheimer disease	5	Fibula	IV	D4e2s2i0g2N1
				6	Tibia	III	d2e1s2i0g1n0
5	80	Female	Stroke, atrial fibrillation	7	Sacrum	IV	d2e2s2i0g1n0

Table 2

Frequency (MHz)	1	3
Intensity		
At ultrasound probe		
SATP (W/cm ²)	1.05	1.70
SATA(W/cm ²)	0.21	0.34
At wound surface		
SATP (W/cm ²)	0.5	0.5
SATA (W/cm ²)	0.1	0.1
Duty cycle (%)	20	20
BNR	3.5	3.2
ERA (cm ²)	5.5	6.0

SATP : Spatial average temporal peak

SATA: Spatial average temporal average

BNR : Beam non-uniformity ratio

ERA: Effective radiating area

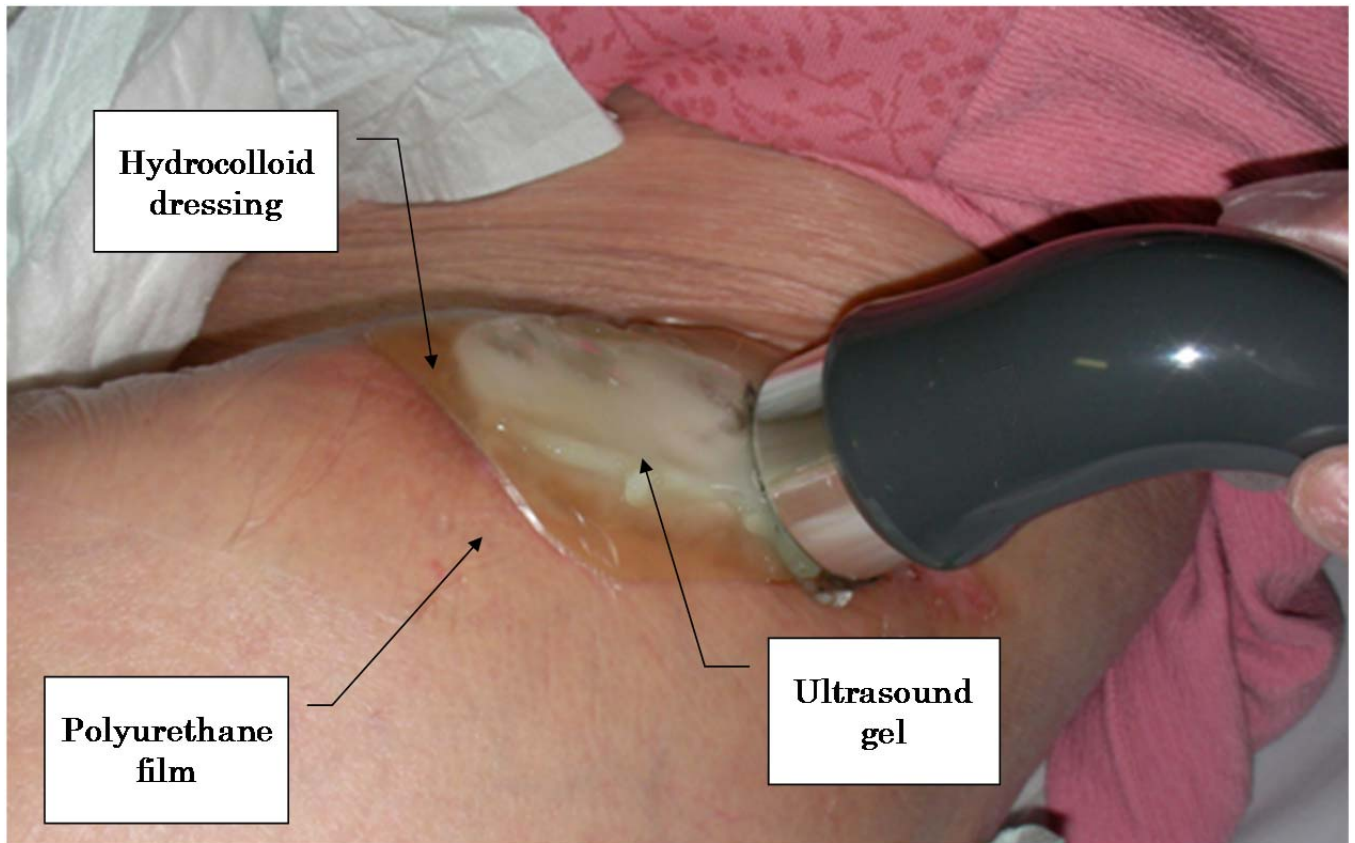


Fig. 1.

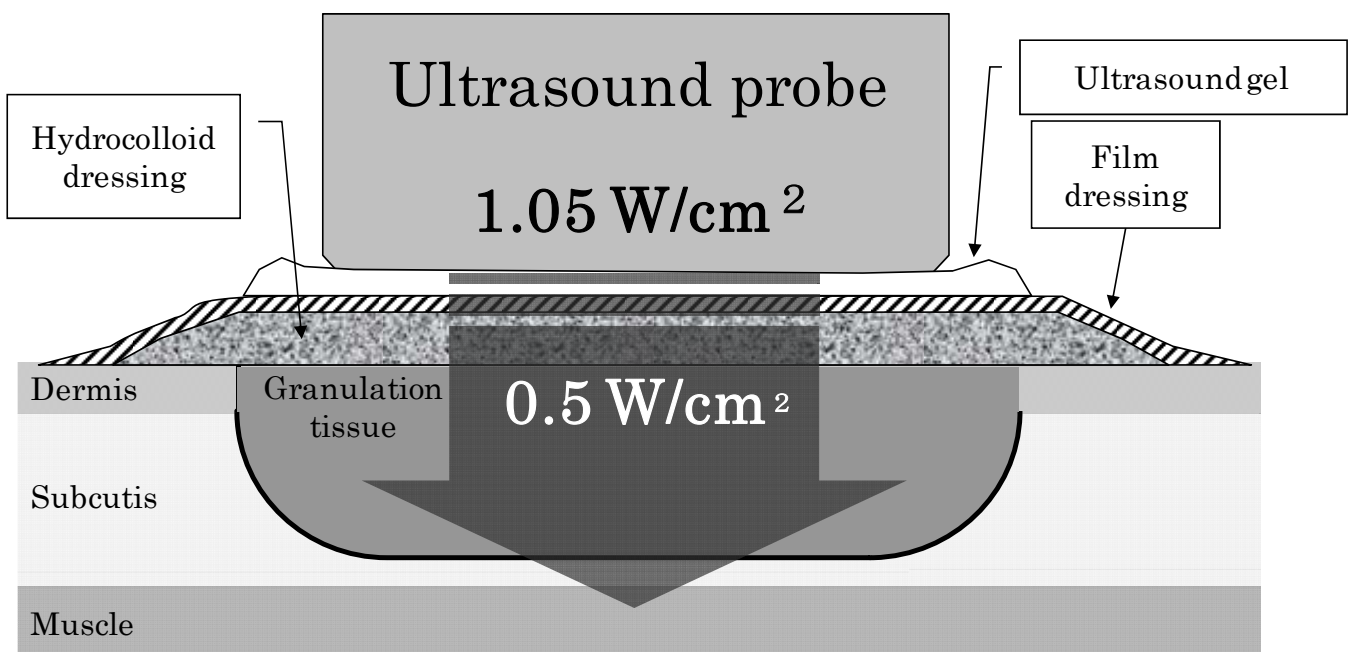


Fig. 2.

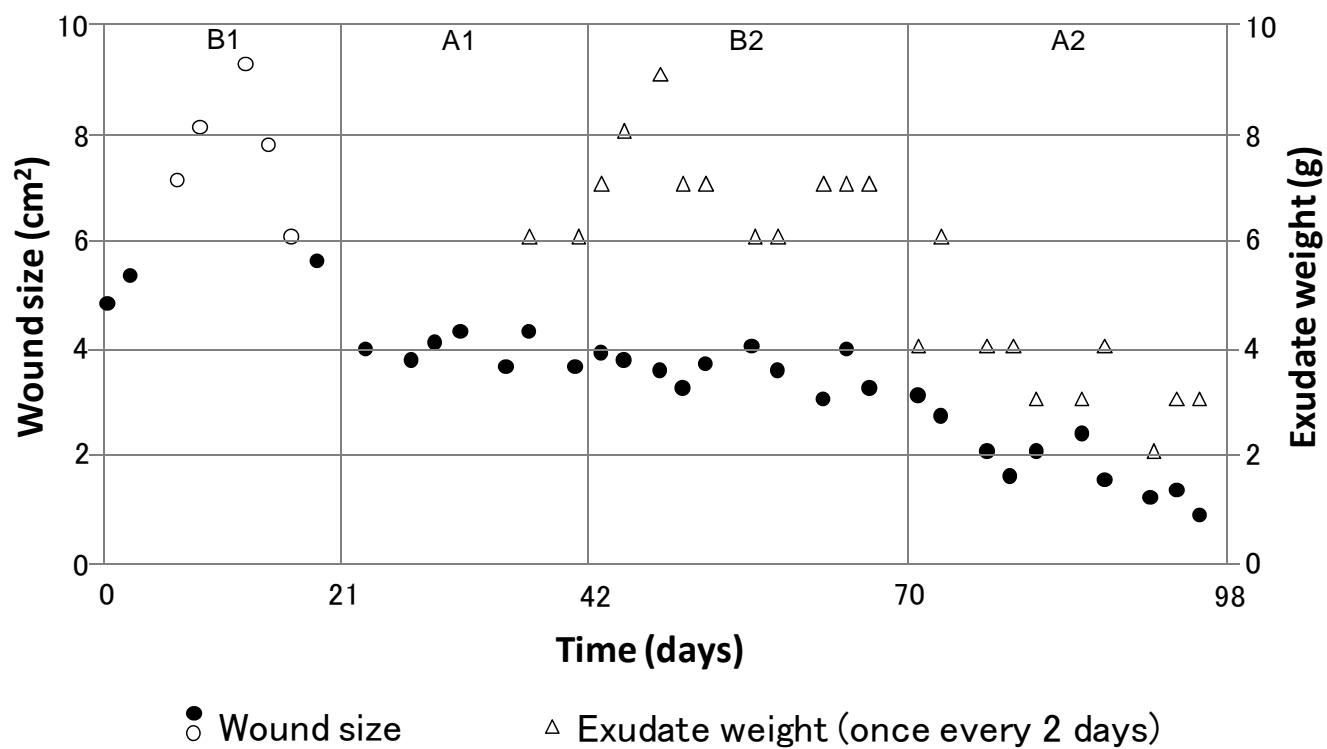


Fig. 3.

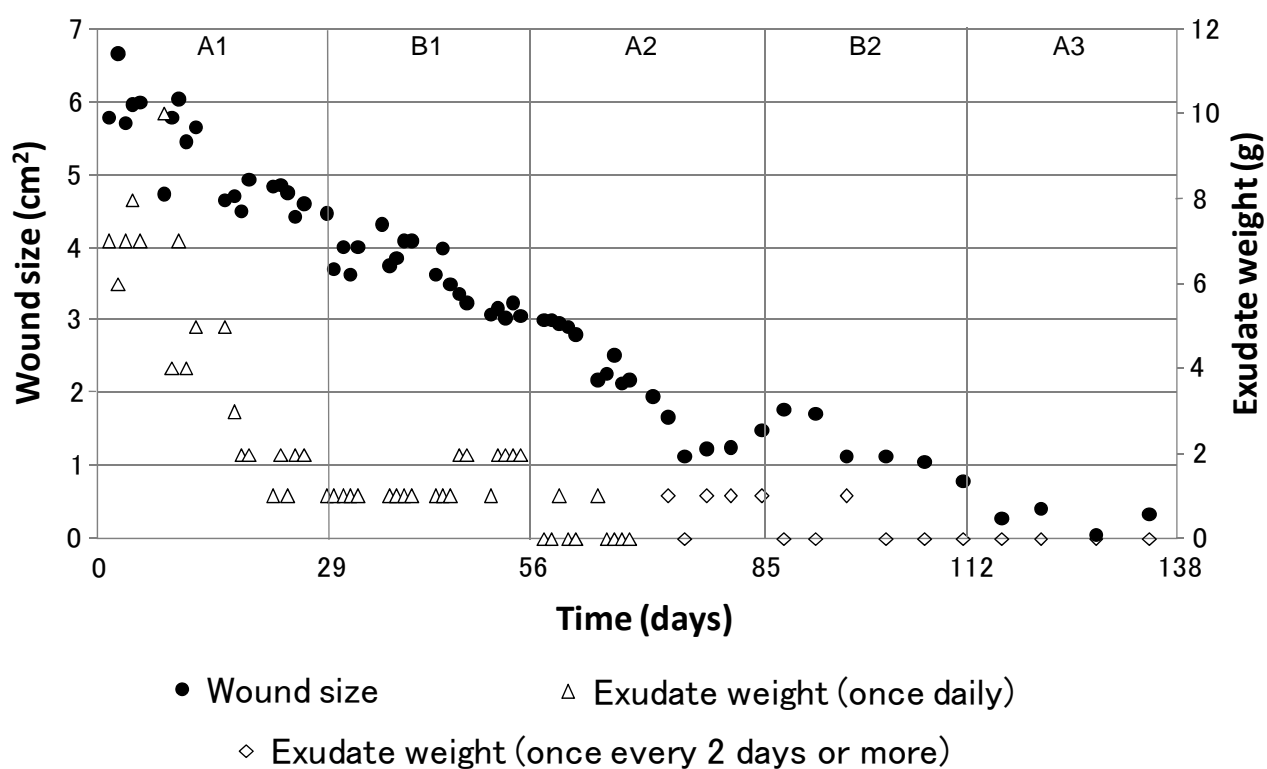


Fig. 4.

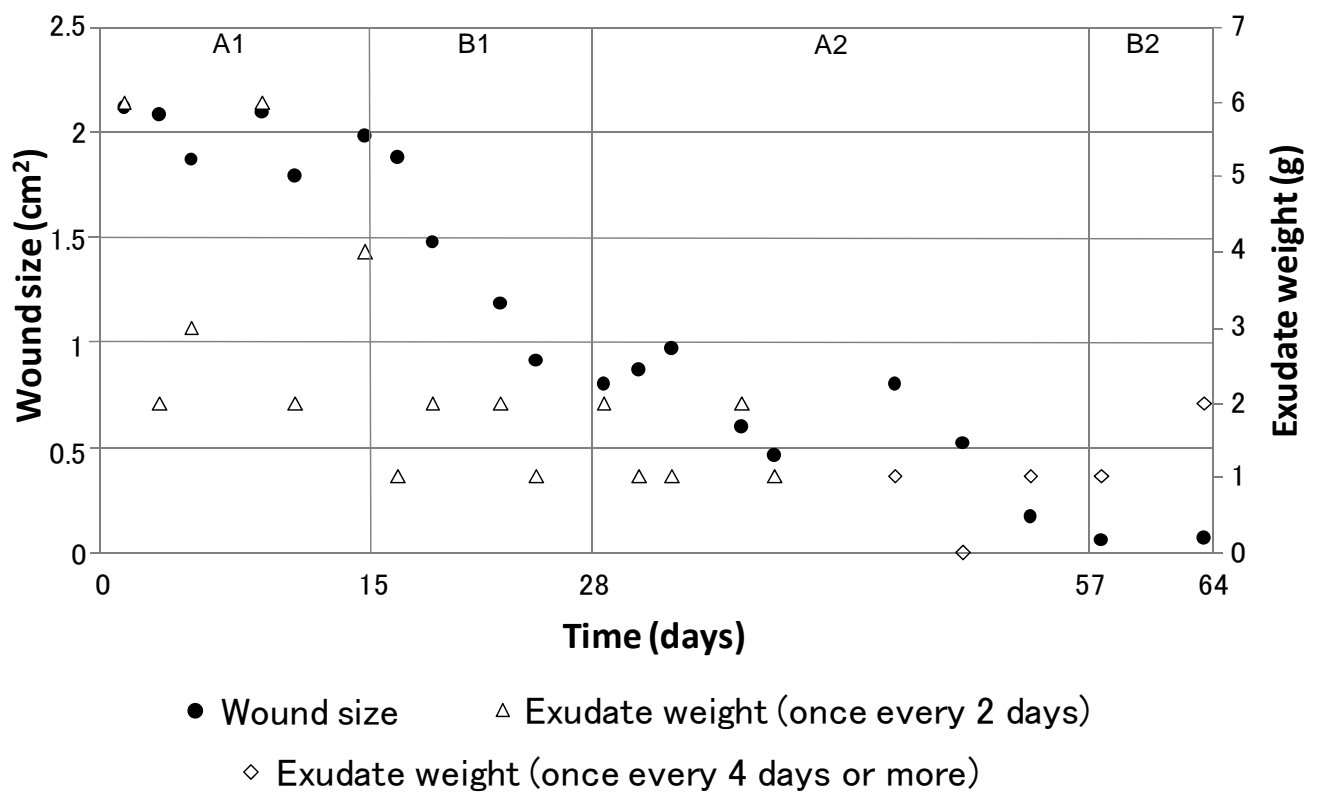


Fig. 5.

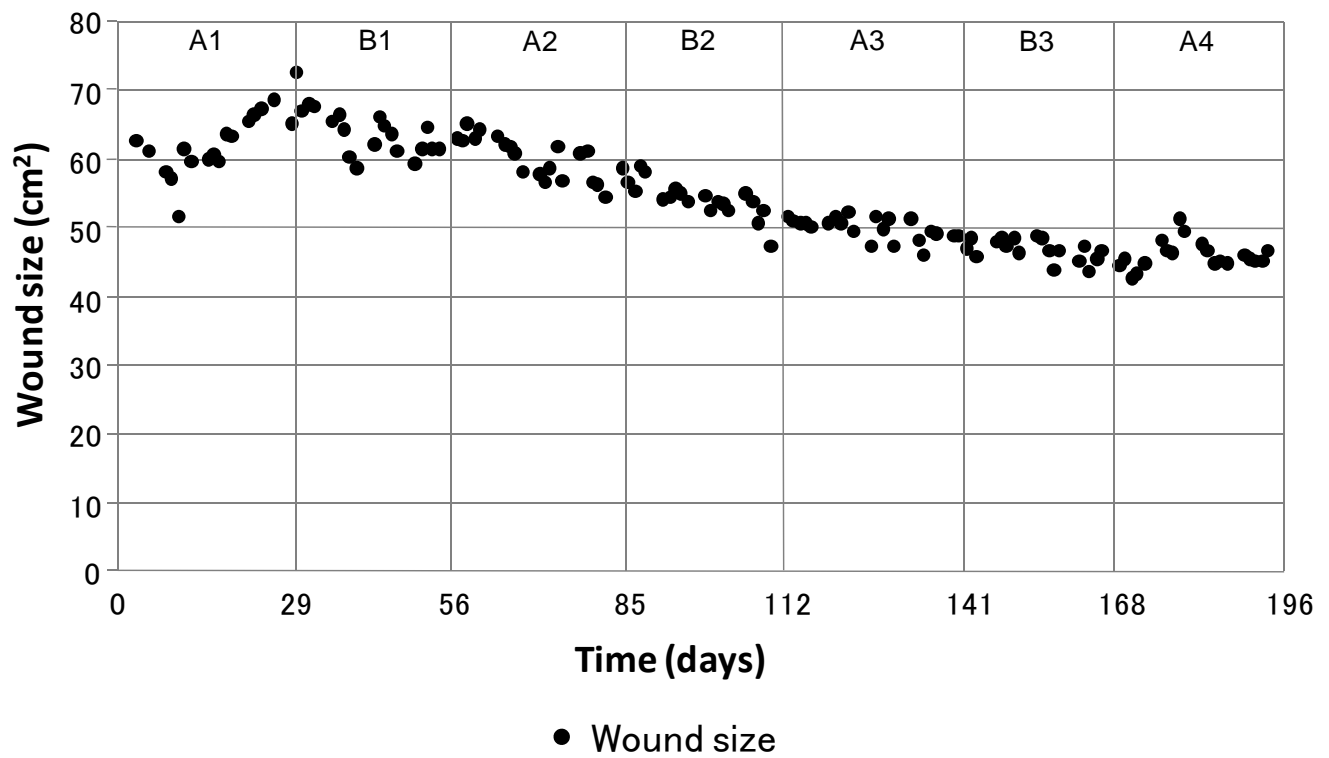


Fig. 6.

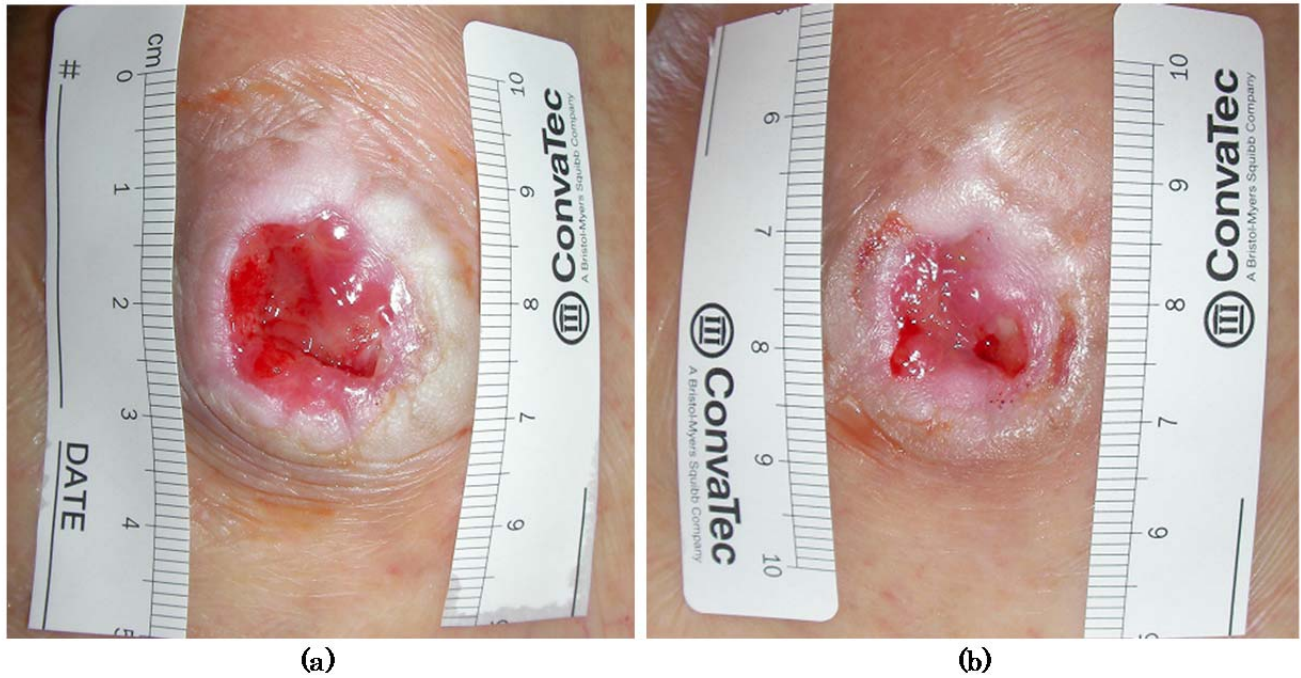


Fig. 7.

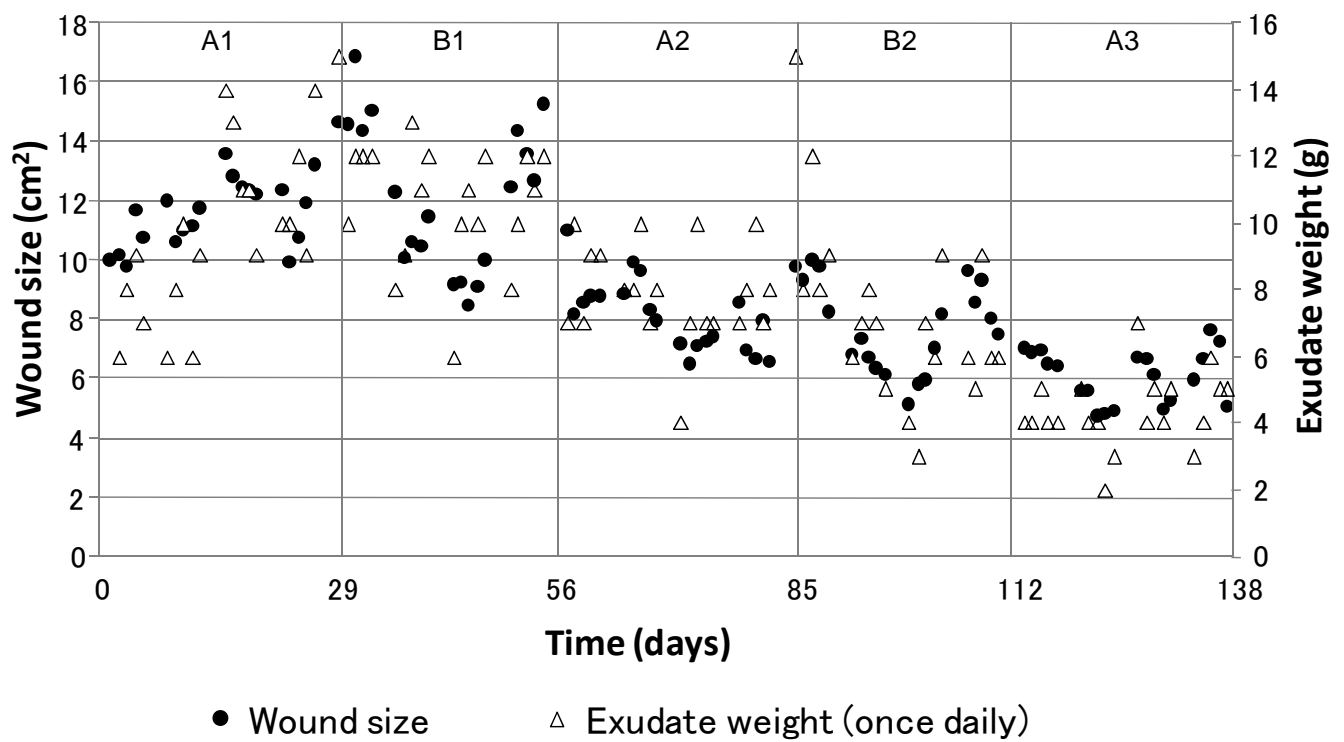


Fig. 8.

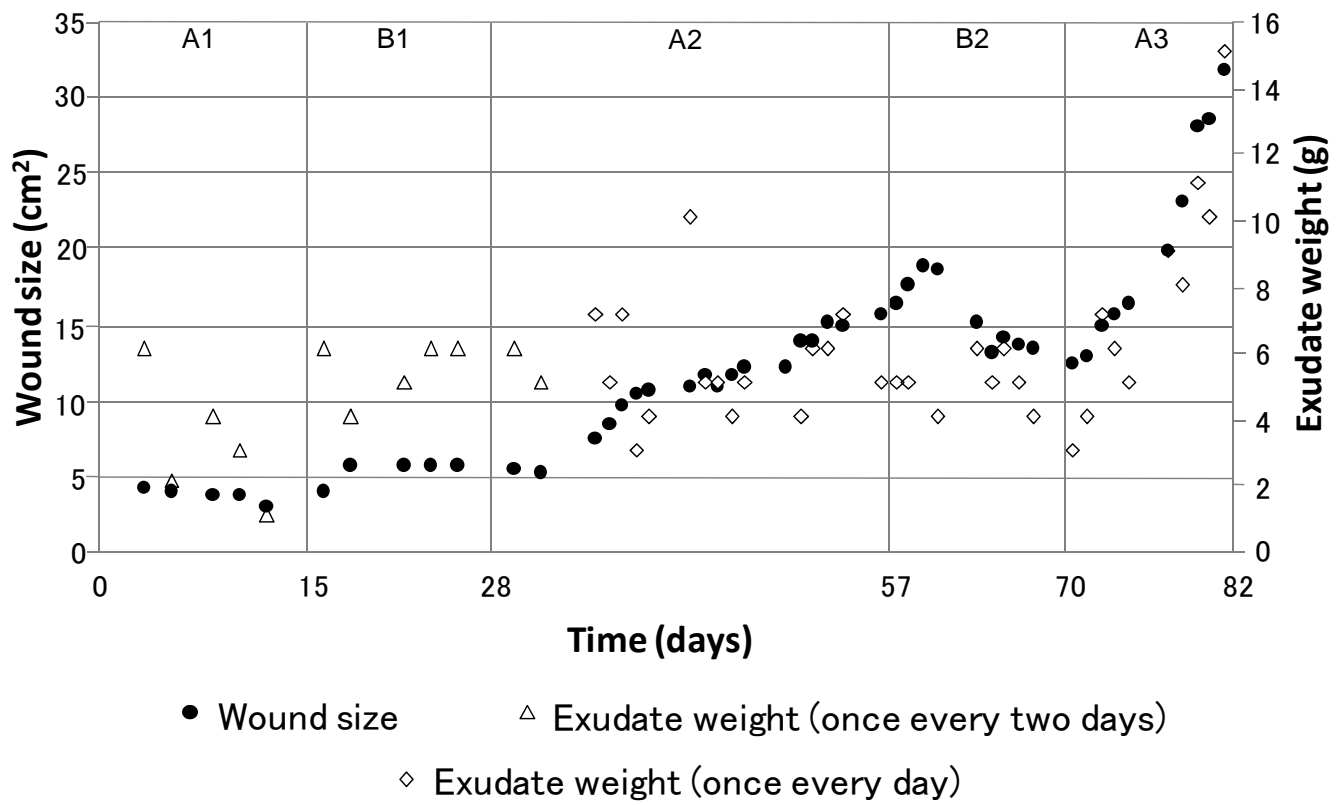


Fig. 9.

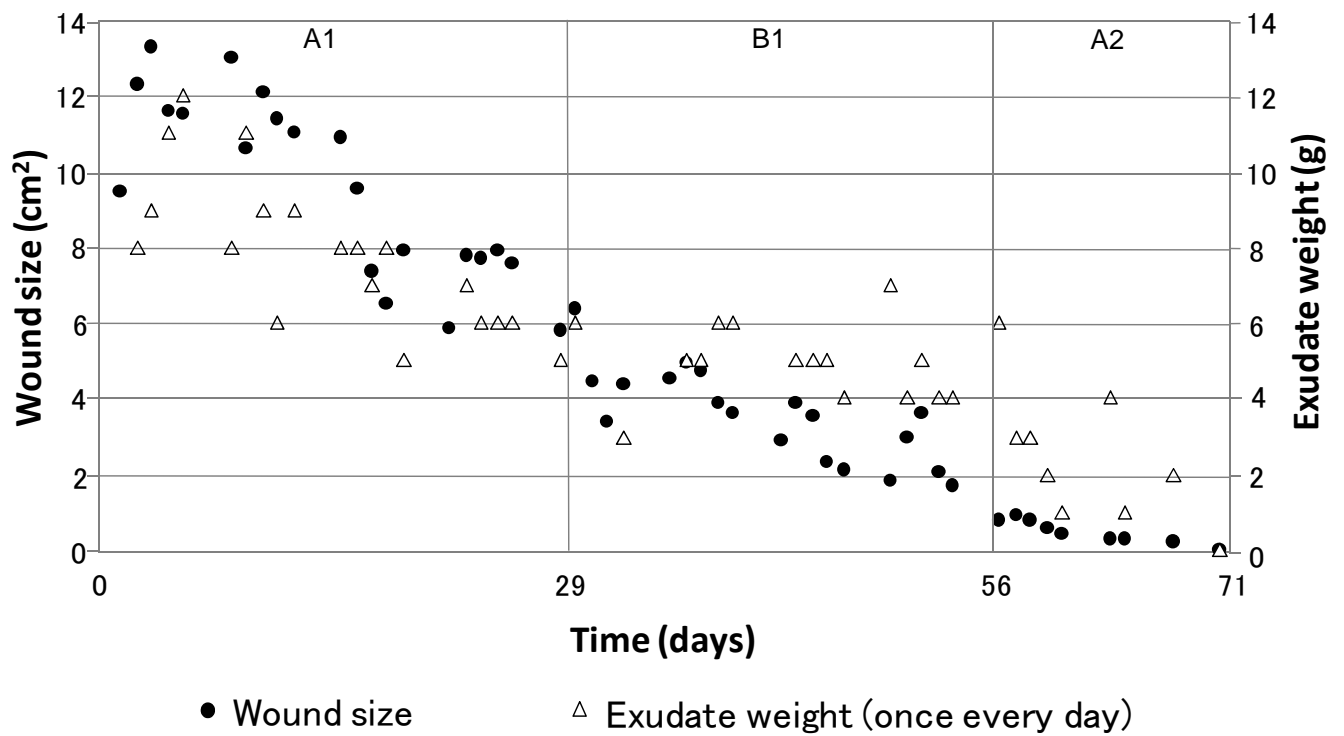


Fig. 10.