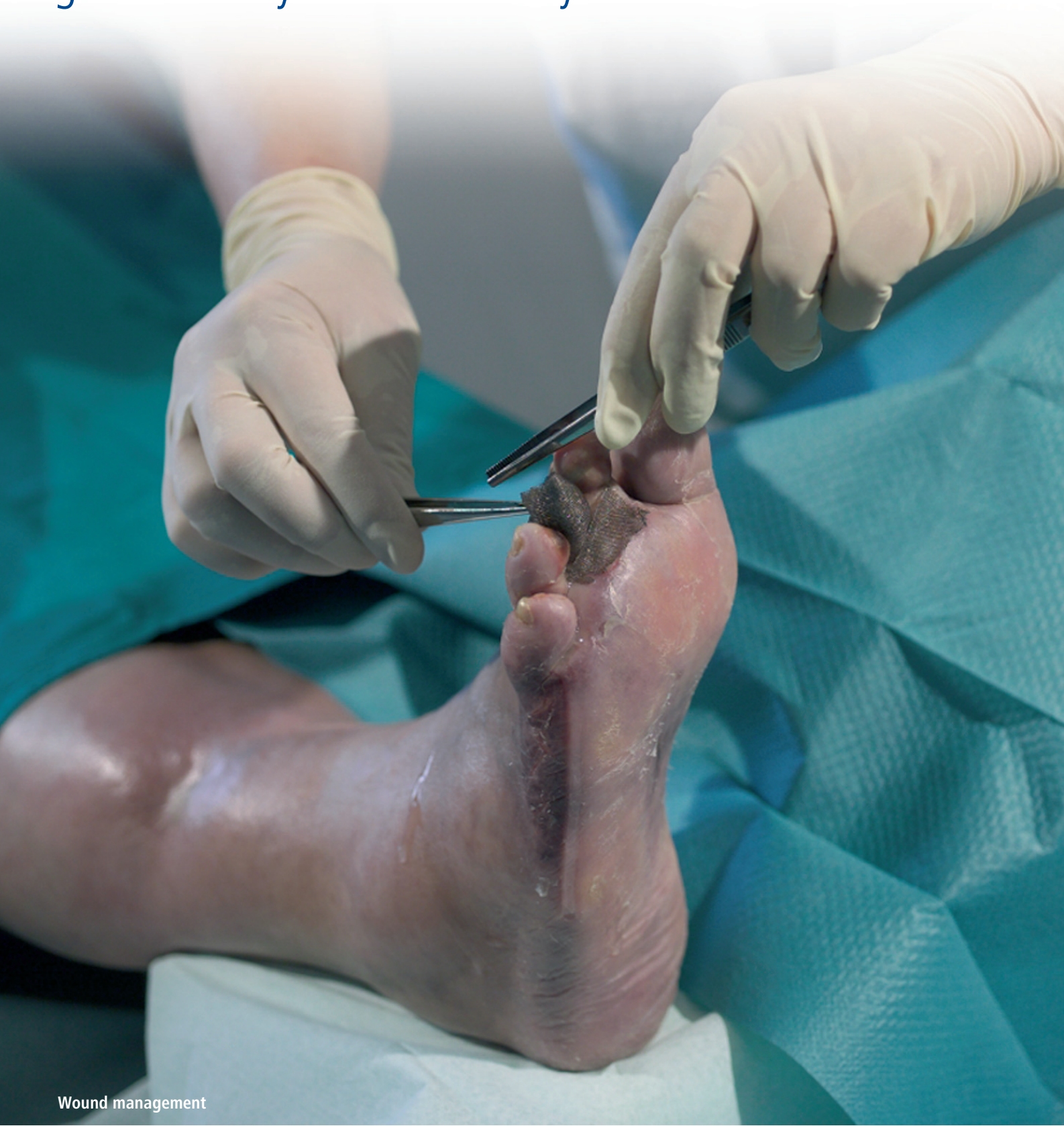
HARTMANN

Treatment of infected and infection-prone wounds with Atrauman Ag

Clinical observation study in 624 patients confirms good efficacy and tolerability



Wound management

Summary

More than 600 patients with predominantly chronic wounds – about two-thirds of them infected – were treated with the silver-containing ointment dressing Atrauman Ag in a multicentre clinical observation study conducted in the outpatient setting. Wound condition improved markedly during the wound treatment which lasted for a mean period of 23 days.

While at the beginning of the study 9% of the wounds were completely and 24.7% extensively covered with a coat of necrotic debris, at the final examination these proportions had decreased to 2% and 0.8% respectively. At the same time, the proportion of wounds without coat increased from 27% to 77%. Wound exudation was also reduced by treatment with Atrauman Ag. The marked decrease in wound coat and exudation was accompanied by an increase in granulation and epithelial tissue.

The number of wounds with moderate, pronounced or complete epithelization increased from 4.5% to just below 45%. Further parameters which improved during Atrauman Ag treatment included wound pain, number of infected wounds and condition of the peri-wound area.

The treatment was tolerated very well by the patients. Both the physicians and patients therefore rated the tolerability of wound treatment with Atrauman Ag as good or very good.

Conclusion: Atrauman Ag is an effective wound dressing for the management of infected and infection-prone wounds and can be used not only in the exudation phase but also in multiple phases of wound healing.

Acute wounds and chronic ulcers are frequently colonized by fecal, oral and dermal microorganisms (1). Since wound flora can become colonized not only with bacteria but also with pathogenic and antibiotic resistant species, depending on the patient's immune status colonization can lead – especially in therapy refractory chronic ulcers – to wound infection (2). In daily clinical practice, methicillin-resistant strains of Staphylococcus aureus (MRSA) present a logistic and therapeutic challenge (3).

A wound infection prolongs the exudative healing phase, resulting in a delay in the overall wound healing process. This has far-reaching consequences for the patient, who not only has to tolerate considerably more pain but also has to anticipate a prolonged treatment period of several months to years until the wound heals completely (4).

Tab.1: Bacterial strains reliably killed by Atrauman Ag

Staphylococcus aureus	DSM 346
Staphylococcus aureus (MRSA)	ATCC 6538
Staphylococcus epidermidis	DSM 2134
Klebsiella pneumoniae	DSM 789
Pseudomonas aeruginosa	DSM 1117
Escherichia coli	DSM 1103
Bacillus subtilis	DSM 347

The silver-containing ointment dressing Atrauman Ag has proved successful both in the primary management of contaminated wounds and in the treatment of chronic ulcers with an elevated infectious risk. When Atrauman Ag comes into contact with exudates it forms silver ions on its metallic surface (see box). The silver ions destroy bacteria on direct contact with the dressing including methicillin-resistant strains of Staphylococcus aureus, which can cause major therapeutic problems in wound infections (5). Since the silver ions are only formed locally within the dressing the cytotoxicity of Atrauman Ag is also very low and the tolerance during treatment correspondingly high.

Atrauman Ag has already demonstrated its clinical efficacy and tolerability in an observation study in 86 patients. These results have now been confirmed in a larger, prospective multicentre clinical observation study involving more than 600 patients with acute and chronic wounds of differing etiology.

Structure and mode of action of Atrauman Ag

The support material of Atrauman Ag is made from a water repellent polyamide textile coated with metallic silver firmly bound to the support material. This in turn is impregnated with a hydrophilic ointment consisting mainly of triglycerides. When Atrauman Ag is applied to the wound, the dressing forms silver ions on its metallic surface on contact with exudate. The silver ion formation is locally restricted to the wound dressing. When bacteria come into contact with the dressing silver ions bind to and destroy these micro-organisms. The wound exudate together with the killed bacteria and the endotoxins formed in the process are absorbed into the secondary wound dressing.

624 patients treated with Atrauman Ag

The prospective, multicentre clinical observation study was performed in the ambulatory setting by 211 physicians – general practitioners, dermatologists, surgeons and internal specialists – and 11 community nursing services, who treated 624 patients with Atrauman Ag and documented the course of wound healing over altogether 2352 visits.

A standardized questionnaire was used to record the patients' age, gender, general state of health and co-existing diseases, the age and size of the wound, previous treatments and concomitant medications. Wound status was evaluated at the initial examination and over the course of the three dressing changes on the basis of the following parameters:

– smeary, purulent coat
– exudation
– wound pain
– granulation tissue
– epithelial tissue

The size of the wound and the state of the peri-wound area were also documented at the beginning and end of the study.

At the end of the observation study, physicians and nursing staff evaluated the efficacy and tolerability and the application characteristics of the silver-containing impregnated tulle dressing. The patients were also questioned about their treatment with Atrauman Ag at the end of the study.

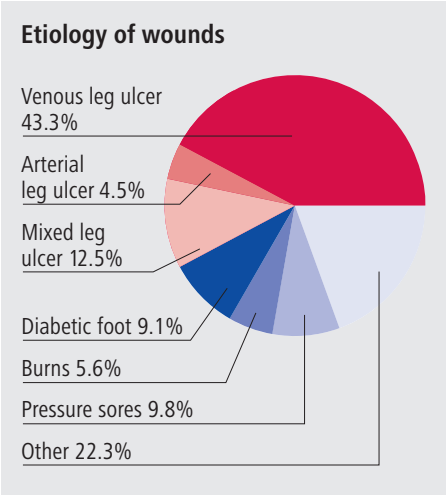


Fig. 1 Etiology of wounds. The majority of the patients were suffering from chronic wounds.

The data recorded on case report forms were analyzed using descriptive statistical methods and the mean values, standard deviations and medians were calculated. Because of missing data, not all the parameters elicited could be included in the analysis. The individual results were therefore calculated using different baseline values. The number of results included in the analysis is shown for each of the parameters.

43% of the patients had chronic venous ulcers

The patients – 61.4% were male, 38.6% female – had a mean age of 70 (±16) years. The physicians reported that just under 14% were in very good and 27.4% in a compromised general condition due to co-existing diseases. Just below 60% were in an age-appropriate physical condition.

The physicians and nursing staff treated patients with chronic and acute wounds of differing etiology (Fig.1). At 43.3% (270 patients), venous leg ulcers were the wounds by far the most commonly treated with Atrauman Ag. This was followed by mixed ulcers (12.5%; 78 patients), pressure sores (9.8%; 61 patients), diabetic foot syndrome (9.1%; 57 patients), burns (5.6%; 35 patients), arterial ulcers (4.5%; 28 patients) and other wounds (22.3%; 139 patients).

The mean age of the wounds was 1.36 years (± 4.5 years). The longest mean age was 3 years for mixed leg ulcer and diabetic foot syndromes and venous leg ulcer at 1.6 years (Tab. 2).

Tab. 2: Age of the wounds, listed according to indication

Indication	arithmetic mean	median	standard deviation
Venous leg ulcer (n = 261)	1.6 years	4 months	4.0 years
Arterial leg ulcer (n = 27)	1.2 years	6 months	1.5 years
Mixed leg ulcer (n = 75)	3.0 years	1 year	7.4 years
Diabetic foot (n = 57)	1.6 years	3 months	1.5 years
Burn (n = 35)	13 days	2 days	1.6 months
Pressure sore (n = 60)	6 months	2 months	1.1 years
Other (n = 136)	11.3 months	1.5 months	5.2 years

Tab.3: Microbial spectrum of infected wounds identified by swab test (multiple responses possible)

Genus	Number of selections
Staphylococcus	60
Pseudomonas	25
Streptococcus	17
E. coli	11
Oxacillin-resistant Staphylococcus aureus (ORSA)	11
Methicillin-resistant Staphylococcus aureus (MRSA)	9
Proteus	9
Enterococcus	7
Acinetobacter	3
Klebsiella	3
Serratia liguefaciens	2
Serratia marcescens	2
Alcaligenes xylosoxidans	1
Citrobacter	1
Corynebacterium	1
Gram-negative microorganisms	1
Gram-positive chain cocci	1
Haemophilus	1
Moraxella	1
Pyocyaneus	1
Mixed infection	2
No information on microbial spectrum	10

Wound dressings previously used for treatment

The treating physicians documented for 463 patients which wound dressings had been used prior to study enrolment. Most of the patients had been treated with impregnated tulle dressings (98 patients), foam dressings (68 patients), hydrocolloids (66 patients), silver-containing wound dressings (60 patients) and wound dressings with antibiotics (59).

Almost two thirds of the wounds were infected

The investigators diagnosed clinical symptoms of infection in more than 60% of the wounds (364 of 600).

For every third infection the diagnosis was confirmed by taking swab samples from the wound. The most frequently detected etiologic agents were staphylococci (in 60 patients), pseudomonads (25 patients) and streptococci (17 patients) (Tab. 3).

Of the 364 infected wounds, 110 were treated with systemic antibiotics (ciprofloxacin, amoxicillin, fusidic acid, clindamycin, doxycyclin etc.).

Concomitant therapies with Atrauman Ag

Two thirds of the patients (365 cases) received pharmacological treatments concurrently with Atrauman Ag; just under one-third (205 patients) received analgesics, 16.5% (103 patients) antibiotics, 6% (39 patients) anticoagulants and 10% (62 patients) other products such as diuretics, antidiabetics etc. The treating physicians also prescribed compression

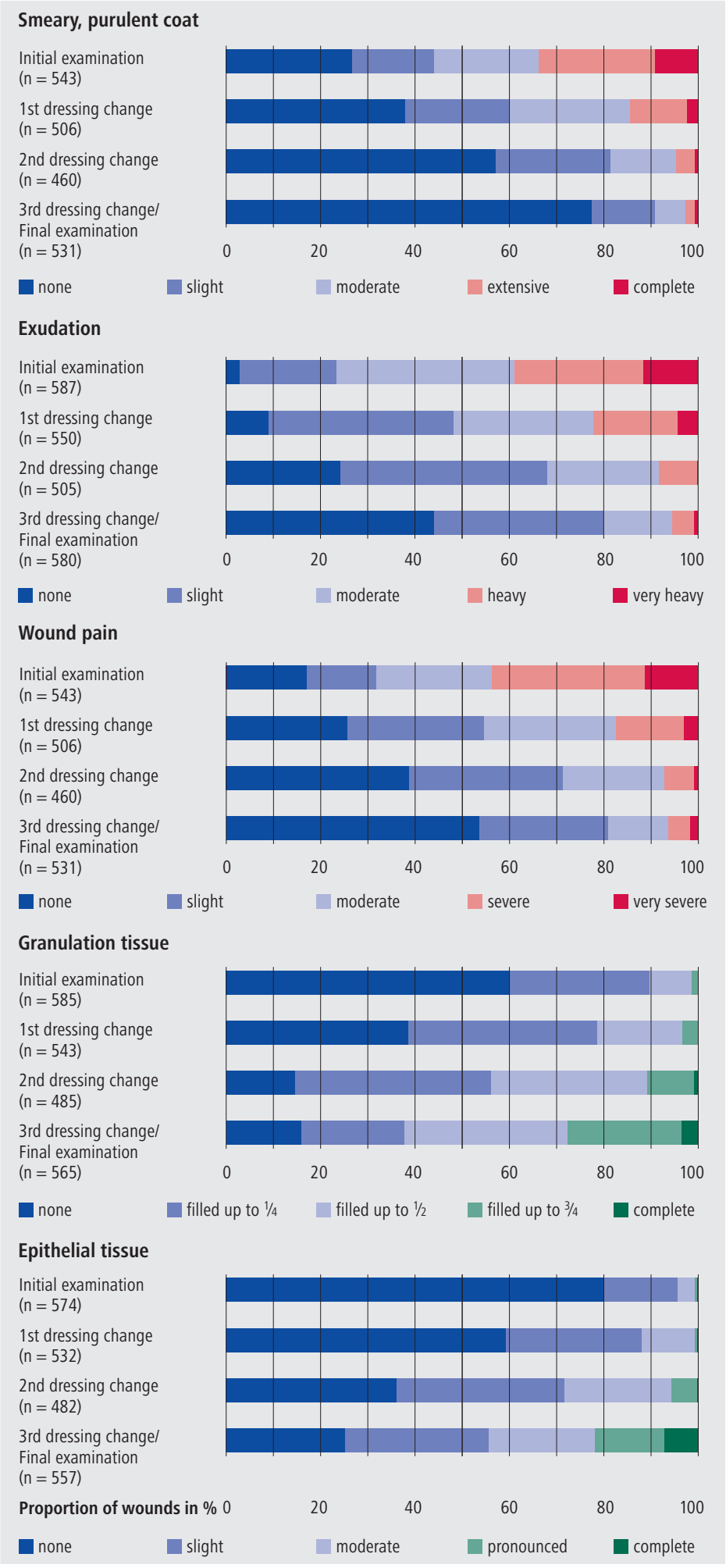


Fig. 2 Development of wound status during the course of the study.

therapy for the 270 patients with venous ulcer and for another 46 patients with a different indication. Further supplementary measures - depending on the diagnosed indication - included pressure relief of the wound, elevation of the legs, special nutritional therapies, physiotherapy etc.

Secondary wound coverage

Atrauman Ag, like all other ointment dressings, is used in combination with a secondary, absorbent wound dressing. The physicians and nursing staff used a variety of products for the dressing, but predominantly traditional wound dressings such as wound dressing pads or gauze swabs (in 411 patients) were used for fixation of Atrauman Ag or wound coverage. Products such as foam dressings, hydrogels, TenderWet or calcium alginates were used, in some cases in combinations.

Number of wounds covered completely or substantially with necrotic debris coats decreased from 35% to 3%

The patients were treated for a mean 23 days with Atrauman Ag, with three dressing changes per patient. Documentation of the course of wound healing showed that the condition of the wounds improved considerably with Atrauman Ag (Fig. 2). While at the beginning of the study 9% of the wounds were covered completely and 24.7% substantially with a smeary coat, this incidence had decreased to only 2% and 0.8% respectively at the final examination. At the same time, the proportion of wounds without coat increased from 27% to above 77%. The degree of wound exudate formation also improved. The number of heavily and very heavily exudating wounds decreased from 39% to below 6% during the course of the study.

The marked decrease in necrotic debris coat and exudation was accompanied by an increase in granulation and epithelial tissue. The proportion of wounds in which no granulation tissue formed on the wound bed, or in which only one quarter of the wound bed was covered decreased from just below 90% to 37% by the end of the observation study. During the same period, the number of wounds with moderate, marked or complete epithelization increased from 4.5% to just below 45%.

Wound pain and infections

The patients also derived direct benefits from the wound healing promoting influence of the treatment. The proportion of patients with severe or very severe wound pain decreased

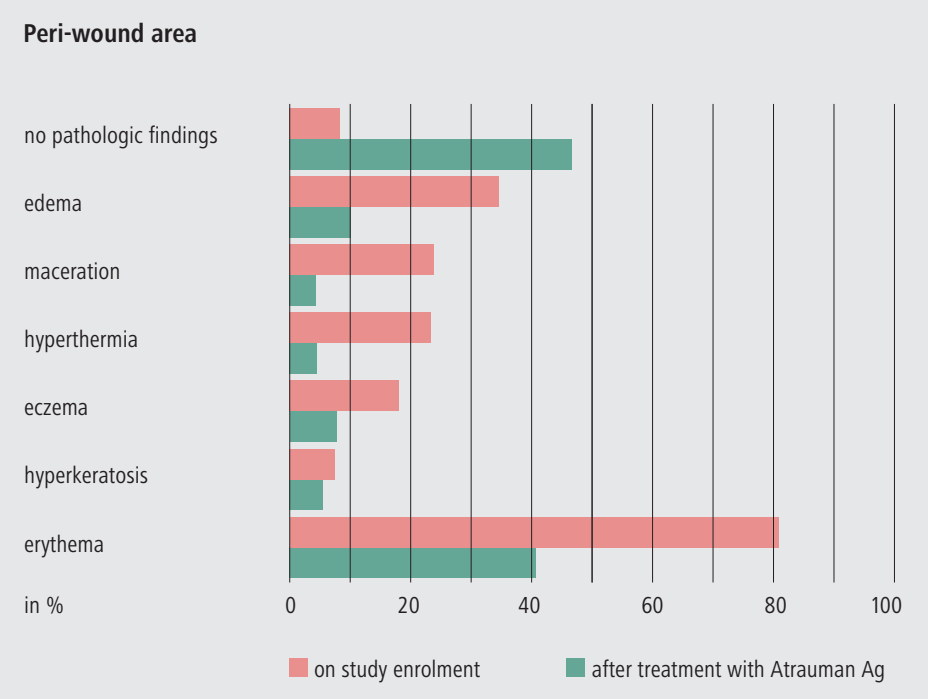


Fig. 3 State of peri-wound area before and after treatment with Atrauman Ag. The proportion of wounds with inconspicuous peri-wound area increased from 8.3% to 46.7% (multiple responses possible).

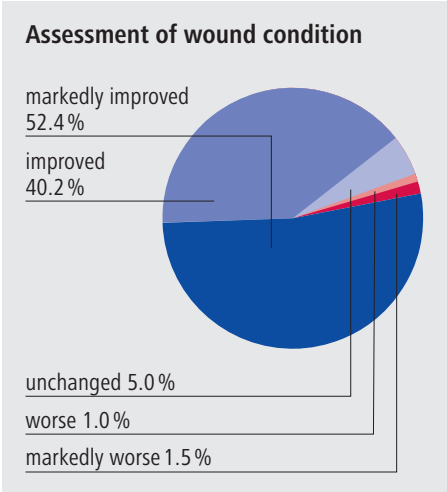


Fig. 4 Assessment of wound status at the final examination (n = 607). More than 90% of the treating physicians reported that the state of the wounds had improved or even markedly improved with Atrauman Ag treatment.

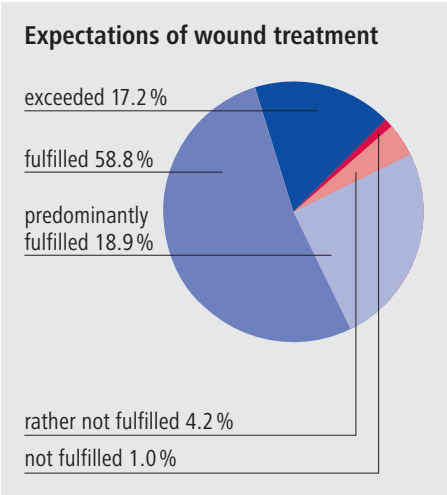


Fig. 5 Expectations placed on wound treatment with Atrauman Ag (n = 594). For 58.8% of the physicians the expectations placed on the wound therapy were fulfilled, for 17.2% they were exceeded.

from just below 40% to 6.5%. At the end of the study 53.5% of the patients reported having no pain. Before the start of Atrauman Ag treatment this was the case for 17%. The marked improvement in wound status and wound pain was accompanied by a decrease in the number of infected wounds.
At the end of the study, 80% of the wounds were free from clinical signs of infection.

Less edema or dermal changes in the peri-wound area

Not only the wound itself, but also the condition of the peri-wound area improved during the course of the study (Fig. 3). For example, the proportion of wounds with inconspicuous wound margins increased from 8.3% to 46.7%, and edema decreased from 34.5% to 10%. At the initial examination, macerations were diagnosed in every fourth patient, and at the end of the study in only 4.3%.

The average wound size decreased from 4.9 (±3.8) cm in length and 3.3 (±2.6) cm in width to 3.5 (±3.6) cm und 2.4 (±2.6) cm, respectively.

Physicians and patients rated the tolerability of Atrauman Ag as very good

Both the treating physicians and the patients were very satisfied with the treatment outcome and the application characteristics of Atrauman Ag. Both emphasized the very good tolerability of the wound therapy, which was rated by over 90% as good or very good (Tab. 4/5). Conformability to the wound bed, ease of removal and application characteristics were rated by more than 90% of users as very good or good. Furthermore, more than 90% were of the opinion that the state of the wound had improved or even markedly improved compared to the initial examination (Fig. 4). Only 2.5% stated that the relevant wound parameters had deteriorated with Atrauman Ag treatment. 17.2% considered their expectations of the treatment had been exceeded and just under 60% regarded them as fulfilled (Fig. 5).

Discussion

Heavy microbial contamination of the wound can greatly influence the wound healing process. Besides an infection confined to the wound area, a growing bacterial burden resulting from a local wound infection can give rise to a systemic infection which may lead to sepsis (6).

The development of silver-containing wound dressings has significantly improved the management of critically colonized and infected wounds (7). Especially for patients for whom systemic antibiotic therapy is not indicated but for whom topical antimicrobial therapy is beneficial, silver-containing wound dressings have a firmly established place. They also offer the possibility of providing additional topical therapy as a supplement to systemic antibiotic therapy.

Compared to antibiotics, silver-containing wound dressings offer the advantage of having only a very slight tendency to induce bacterial resistance, even over long periods of use (8). The silver ions responsible for the bactericidal action, however, are also toxic for the cells in the wound area (9). Silver-containing wound dressings should therefore only form as many silver ions necessary to produce an effective bactericidal action. The silver-containing ointment dressing Atrauman Ag was developed in accordance with this concept since its antibacterial effect is restricted to the dressing. Clinical studies and laboratory tests have already demonstrated the beneficial profile of action of low toxicity and potent antimicrobial action (Ziegler et al, Skin Pharmacology and Physiology, printing). These results have now been confirmed in the present large-

Tab. 4: Assessment of Atrauman Ag use by treating physicians

	very good %	good %	satisfactory %	adequate %	poor %
Conformability to wound bed (n = 613)	49.3	44.7	5.7	0.3	0
Ease of removal (n = 612)	60.8	35.9	2.6	0.5	0.2
Tolerability (n = 609)	56.5	38.3	2.3	0.8	2.1
Application characteristics (n = 612)	51.5	45.6	2.6	0.3	
Overall impression (n = 609)	42.0	52.5	3.8	1.5	0.2

Tab. 5: Assessment of wound treatment with Atrauman Ag by patients

	very good %	good %	satisfactory %	adequate %	poor %
Tolerability (n = 601)	60.9	32.8	3.3	0.3	2.7
In-use comfort (n = 601)	54.9	39.1	4.3	0.8	0.8
Overall impression (n = 599)	52.1	40.9	4.8	0.3	1.8

scale, prospective multicentre clinical observation study conducted in the outpatient setting.

Most of the patients were suffering from therapy refractory ulcerations – 60% of the wounds had no granulation tissue on study enrolment, almost 80% had formed no epithelial tissue – of the type frequently encountered in daily clinical practice. Furthermore, a large proportion of the wounds were infected and extensively covered by smeary purulent coats. Just under two thirds were producing large amounts of wound exudate. Treatment with Atrauman Ag markedly improved the condition of the wounds. During the course of the three dressing changes, the investigators diagnosed many fewer wound coats and much less exudate, while at the same time the proportion of granulation and epithelial tissue increased. The number of infected wounds also decreased. In the view of the treating physicians, 90% of the patients had experienced a marked or even very marked improvement in the condition of their chronic wound compared to the initial examination.

Atrauman Ag, like all other impregnated tulle dressings, is combined with a secondary absorbent wound dressing. Both laboratory tests and clinical practice use have demonstrated the effective bactericidal and wound healing promoting properties in combination with numerous hydroactive and traditional wound dressings. The user can therefore select a suitable secondary dressing depending on the state of the wound. It is also possible to continue using the previous wound dressing if supplementary treatment with Atrauman Ag is temporarily indicated.

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Conclusion

Atrauman Ag is an effective wound dressing also for the management of infected and infection-prone, treatment refractory ulcers and can be used not only in the exudation phase but also in multiple phases of wound healing. Since the silver ions are only formed locally within the dressing the cytotoxicity of Atrauman Ag is also very low and the tolerance during treatment correspondingly high.

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