Ultrasound and the Treatment of Pressure Sores

T McDIARMID MSc MCSP

Department of Rehabilitation,
University of Southampton

P N BURNS BSc PhD

Department of Medical Physics,
Bristol General Hospital

G T LEWITH MA MRCP

Primary Medical Care,
University of Southampton

D MACHIN MSc

Community Medicine and Medical Statistics,
University of Southampton

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Summary: The paper reviews the natural history and treatment of pressure sores and describes a preliminary double-blind randomised trial to test the efficacy of ultrasound therapy on this condition. It was found that although ultrasound appears to be of value in the treatment of pressure sores, the complexity of other factors involved in their healing means that a large trial involving more than 1,000 patients would be needed to demonstrate this in a statistically valid manner. Infected sores heal more slowly than clean ones. While no effect of ultrasound on clean sores was observed, ultrasound therapy appeared to improve the rate of healing of infected sores. The mechanism for this effect merits further investigation.

Biography: Theresa McDiarmid qualified at Guy's Hospital, London in 1974. She then worked at Nevill Hall Hospital, Abergavenny before joining Bristol and Weston Health Authority. While gaining senior clinical experience in general physiotherapy fields, she developed an interest in ways of determining the efficacy of various treatment regimes. She went on to pursue this at the Department of Medicine, University of Southampton, where she was awarded the MSc in Rehabilitation Studies in 1983. She then worked for one year as superintendent of Keynsham Hospital, Avon, before moving to Connecticut, USA, where she is currently involved in the development of back care and sports injuries programmes.

Dr Peter Burns graduated from the University of Sussex in 1974 with first-class honours in theoretical physics. He has been working as research physicist in the Ultrasonics Unit of Bristol General Hospital since 1978. His interest there has been principally in the development of new techniques in diagnostic ultrasound, though he is also involved with its therapeutic applications. He is currently research associate in diagnostic radiology at Yale University School of Medicine, USA, where he is working on the non-invasive measurement of human and fetal blood flow using Doppler ultrasound.

Dr George Lewith is currently director of the Centre for the Study of Alternative Therapies, Southampton, a centre involved in teaching and research in various areas of complementary therapies. Previously a lecturer in primary medical care at the University of Southampton, Dr Lewith has been involved in supervising research projects on the MSc course for the Department of Rehabilitation Studies at the university for five years.

Mr David Machin is senior lecturer in medical statistics, Community Medicine and Medical Statistics, The University of Southampton Faculty of Medicine.

Introduction

IT is estimated that at any one time there are about 30,000 hospital patients in England and Wales affected by pressure sores (Kenedi *et al*, 1976). This represents about 8% of the hospital population. The existence of such a widespread problem exacts a considerable toll on the medical and financial resources of the National Health Service, both through expensive labour-intensive treatments and the delay in rehabilitation of the sufferers.

As the condition is widespread and its effects costly, prevention and treatment deserve careful examination. There are numerous approaches to the problem, ranging from the patho-physiology and biomechanics of the ulcer's origin to the pharmacology and biophysics of its treatment. Increasingly, physiotherapists are called upon to contribute to the treatment and they have a growing array of techniques at their disposal. However, until there is an adequate understanding of the underlying processes and the actual effect of treatments used in what is so often a complex clinical condition, it will be difficult for physiotherapists to offer a useful contribution to the patient's management.

In this paper it is hoped to show that it is possible to assess the effects of physical therapy in a real clinical setting, in spite of the large number of uncontrollable variables. Attention is focused on one such therapy — ultrasound — and the relationship examined between its effectiveness and the presence of other clinical factors. To understand the relevance of these factors, though, it is necessary first to review the natural history of pressure sores.

Pressure Sores

The term 'pressure sore' is used to describe any localised area of tissue necrosis resulting from ischaemia in skin and subcutaneous tissue subjected to pressure. This pressure generally is between an underlying bony prominence and some overlying compressive force. As the various layers of subcutaneous tissue respond differently to mechanical forces, vascular obstruction with resulting ischaemia of soft tissue in the area can be caused in a variety of ways. For example, direct pressure can cause compression, while friction or shearing forces (such as between bedding and the sacrum in the semi-recumbent position) can place blood vessels in superficial tissues under stretch and angulation and thereby cause occlusion

Ischaemia, produced for a short period of time or by mild pressure, is sometimes compensated by a reactive hyperaemia once the pressure is removed. However, if the pressure persists for longer than a certain time or is beyond a certain magnitude, irreversible pathological changes occur. These consist of loss in skeletal muscle of cross striations and myofibrils, hyalinisation of muscle fibres, neutrophilic infiltration and phagocytosis by neutrophils and macrophages. Venous thrombosis may also occur in larger vessels in the area, resulting in prolonged circulatory embarrassment even after the pressure has been relieved.

Healing

The normal healing process has been described by Barton and Barton (1981) and can be considered in three stages:

Stage 1: Inflammation and debridement. This is where necrotic debris must be removed in order to provide a clean area for cell migration and division. Local tissue response to damage involves the production of a fibrinous exudate in which polymorphonuclear leucocytes can move and multiply in order to carry out phagocytosis. One of the processes involved is digestion of the dead tissue by enzymes released from the lysosomes of the macrophages. This, along with dead leucocytes, forms pus which must be absorbed or removed if healing is to occur.

Stage 2: Proliferation. This stage involves wound contraction and epithelialisation. Wound contraction is the reduction of all or part of a skin defect by centripetal movement of the surrounding skin. The visco-elastic properties of skin on which it depends rely on the growth of blood vessels and tissues into the contracting margin of the sore. This process is thought to be due either to physical alterations in collagen or protein components of the intercellular matrix or to the physical activity of fibroblasts and myofibroblasts countering skin tension. The process is hindered by cellular toxins or any mechanical obstruction, such as dry slough, dry dressings or excessive fibrosis. Epithelialisation depends on moisture for cell migration, cleanliness and wound stability.

Stage 3: Remodelling. The strength and permanence of the repair are largely determined early in the process when the new cells are being laid down. This stage can last for several months as the scar tissue matures, with vascularity decreasing and strength increasing as collagen is absorbed in some locations and synthesised in others so as to produce a more organised network of fibres.

Prognostic Factors

The progress of the above processes depends on factors which influence the state of soft tissue viability and its capacity to heal. These factors can be divided into two groups:

1. Intrinsic factors. These relate to the patient's internal condition and to his or her physiological ability to heal; for example, cardiovascular state, nutritional state or motor or sensory deficit.

2. Extrinsic factors. These relate to the environment in which the healing must occur; for example, local pressure, temperature, moisture.

It is evident that, once established, pressure sores can present quite a complicated set of clinical problems. The most obvious solution, of course, is prevention. This is achieved by avoiding sustained or excessive pressure over a small area of the body surface, as well as maintaining vulnerable tissue in as robust a condition as possible.

Treatment

Despite such attempts, however, pressure sores may still appear. Tissue damage can, of course, occur before hospital admission; for example an elderly patient may fall at home and be found several hours later suffering from shock, dehydration, anaemia and unrelieved pressure. Damage may also occur in hospitalised patients with extreme illnesses in spite of appropriate preventive precautions.

To treat a sore, the pressure must first be relieved and the care of the wound considered. Here the aims are to encourage debridement and proliferation. Numerous systemic and topical agents have been used in the belief that they will hasten these processes. The efficiency of few of the agents has been assessed objectively and treatment often appears based more on traditional practice than on sound physiological considerations. For example, many people believe that drying a wound will hasten its healing. Winter (1976), however, has shown that a clean wound with an occlusive dressing will heal 50% more quickly than a dry wound because of the moist environment needed for cell migration and wound stability.

Physiotherapy treatments also attempt to encourage debridement and proliferation. Abiotic doses of ultra-violet radiation are used in an attempt to destroy superficial bacteria in an infected sore as well as reinforce the body's normal mechanism for destroying bacteria (Scott, 1971). Healing is also thought to be encouraged by increasing the flow of blood to the area of the wound. To this end, biotic doses of ultra-violet radiation, ice, infra-red radiation, short-wave diathermy (continuous and pulsed), interferential therapy and massage are used.

There have been few convincing attempts to test the effectiveness of these treatments. Moreover, when considering the physiology of healing it is obvious that some of these treatments might not only be useless (for example, if a patient is uraemic) but may actually delay healing, for example by the drying effect of ultra-violet and infra-red therapy, the physically damaging effect of massage on already devitalised tissue (Dyson, 1978) or the prolonged inflammatory reaction provoked by ultra-violet therapy, if given at the wrong stage of healing (Tepperman *et al,* 1977).

Ultrasound Therapy

There is, however, scientific evidence that another physiotherapeutic mode of treatment should favourably affect the healing process, both in the rate and quality of the healing. Ultrasound therapy (US) affects soft tissues in ways very different to those mentioned above, invoking biological mechanisms which, although not yet fully understood, hold promise for a considerable advance over other treatments. In order to judge such effects, careful assessment must be made because of the many factors involved.

Therapeutic ultrasound produces a wide range of biological effects. Recent work into the mechanism of these phenomena has shown that there exist non-thermal effects whose origin is quite distinct from the thermal or heating effect of ultrasound (Dyson *et al,* 1968; Wells, 1977). Those effects thought to be biologically important are stable cavitation and acoustic streaming. Both of these are consequences of the formation of tiny (micron size) bubbles in soft tissue which may vibrate or move under the influence of the acoustic field. The motion of such bubbles can alter, for example, the function of a cell membrane. Those biological processes which have been found to be specifically affected by ultrasound include:

1. General protein and collagen synthesis by fibroblasts (Harvey *et al,* 1975; Webster *et al,* 1978, 1980).
2. Fibroblast motility (Miller *et al,* 1978).
3. Fibroblast ultrastructure (Dyson and Pond, 1970).
4. Permeability of fibroblast membrane (Harvey *et al,* 1975).
5. Lysosomal fragility (Taylor and Pond, 1972).
6. Tensile strength and elasticity of scar tissue (Dyson *et al,* 1979).
7. Modification of contraction in skin wounds (Dyson *et al,* 1981).

This work has shown that ultrasound can affect biological material in a way that will improve the quality of regenerated tissue as well as its rate of production. There continues to be discussion over which physical mechanisms are involved in the specific changes. It is also becoming apparent that ultrasound can affect tissue repair in different ways depending on the stage of repair and the exposure parameters (Pospisilova, 1976; Dyson, 1984a). It is widely agreed, however, that it is the non-thermal effects produced by ultrasound that are most significant in the stimulation of tissue repair. This, therefore, gives ultrasound a unique place in the physiotherapeutic treatment of soft tissue wounds.

As scientific work continues in the attempt to identify and understand the exact processes involved in the effects of ultrasound on healing, clinical work should proceed. There have apparently been no damaging side-effects from ultrasound treatment when correctly applied.

Thus far there has been little definitive work on the effect of ultrasound on healing in the clinical situation. Dyson *et al* (1976) found that ultrasound significantly increased the rate of healing of varicose ulcers. More than 20 years ago, Paul *et al* (1960) made the clinical observation that ultrasound was 'markedly effective in relieving congestion, cleansing necrotic areas and promoting healing with healthy, non-adherent skin approaching normal thickness' and 'that it would appear that a scientifically controlled study in this area would be richly rewarding'. Given the *in vivo* and *in vitro* evidence accumulated since this statement was made, it would appear long overdue that his recommendation was followed.

Method

Patients with pressure sores were referred by physiotherapy and nursing staff in three Bristol hospitals. Although certain exclusions were felt to be necessary, the criteria for acceptance were made as broad as possible so as to obtain a clinically relevant group of patients. The criteria were:

1. The sore was considered to be a result of pressure and limited to the superficial tissues not extending beyond the dermis.
2. Patients were over 18 years of age.
3. Pressure on the sore was capable of being removed.
4. There was no malignancy in the area to be treated.
5. There had been no radiotherapy in the area in the last six months.
6. There was no evidence of deep vein thrombosis in the area.

Information from the medical and nursing notes concerning the patient's medical history and physical condition was recorded, so that the intrinsic factors affecting healing could be assessed. Details of the extrinsic factors affecting the patient were also taken in the same way as for the Norton score (Norton *et al*, 1962). This is a numerical index intended to reflect the likelihood of a patient developing a pressure sore. The score is calculated on the basis of such factors as the patient's physical activity, mental state, mobility and continence. Finally, details of the pressure sore itself were noted: the site, date of onset, whether it was clean or infected, any dressings or medicaments used, its progress and the extent to which surrounding skin was affected.

Patients were then randomly allocated a number which placed them in either the ultrasound treatment group (US) or the group receiving the mock ultrasound placebo treatment (mock-US). The ultrasonic generator was modified so that the number could be entered on a dial causing the machine to function or not according to the randomisation code. This code remained unbroken until the end of the trial so that the investigator did not know which group the patient was in. As there are no sensory or visible physical effects from ultrasound therapy, the patients were also unaware in which group they were placed. Thus the treatments were double-blind.

A Therasonic 1030 generator (Electro-Medical Supplies Ltd, Oxon) was used to administer the treatments following initial calibration of acoustic power and beam shape by the National Physical Laboratory. During the trial the acoustic output was checked at regular intervals using a simple radiation pressure balance (Burns and Pitcher, 1984). The relevant treatment parameters are shown in table 1.

Table 1: Ultrasonic treatment parameters

ultrasonic frequency:	3 MHz
spatial average temporal peak intensity:	0.8 W cm^{-2}
pulse duration:	2 ms
duty factor:	0.2
spatial average temporal average intensity:	0.16 W cm^{-2}
effective radiating surface area:	5.2 cm^2
duration of treatment:	minimum of five minutes for all pressure sores up to 3 cm^2. One additional minute was added for each additional 0.5 cm^2, maximum ten minutes
frequency of treatment:	three per week

To assess progress of the sores, the margin of granulating tissue was traced on a transparent film placed over the sore. Ten tracings were made for each measurement. Initially these tracings were digitised on the pattern of a microcomputer and the mean area calculated to a precision of a few square millimetres. However, the simpler method of estimating the area by multiplying the maximum length by the maximum perpendicular breadth (equivalent to approximating the sore perimeter to an ellipse) produced essentially equivalent results (McDiarmid, 1983). The use of a computer for planimetry of these sores is not, therefore, essential. The sores were examined clinically before randomisation and classified as either clean or infected. No bacteriological investigations were undertaken.

Results

Forty patients were entered into the trial and approximately 300 treatments were given. The progress of the individual sores is summarised in table 2. Only 18 patients could be followed until their sores were completely healed. The sore survival time was then used as the measure of treatment efficacy. The remaining 22 patients gave 'censored' sore survival times caused by either death, discharge or the sore not being closed before the end of the trial. There were five males in each treatment group and the average age of the patients was 80 years.

Table 2: Patient progress during the trial

Condition of sore at last observation	*Patient status*	*US*	*Mock-US*	*Total*
Healed		10	8	18
	Discharged	6	1	7
Unhealed	Death	2	4	6
	Trial closed	3	6	9
Total		21	19	40

The method of analysis by means of the log rank test is that described by Peto *et al* (1976, 1977). In figures 1 and 2 the vertical axis represents the fraction of unhealed sores while the horizontal axis represents the pressure sore survival, that is, the time to complete healing in days from randomisation.

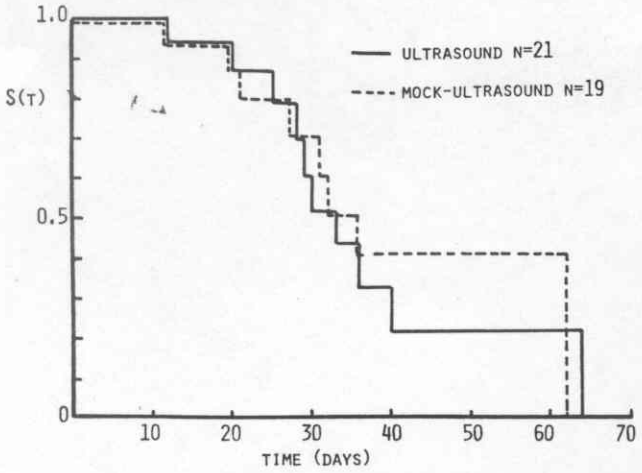

Fig 1: Life table survival curves for pressure sores treated with ultrasound and mock ultrasound (S(T) is the proportion of unhealed sores)

From figure 1 it can be seen that the insonated sores tended to heal more quickly than the mock-insonated sores. The corresponding median healing times were 32 and 36 days respectively. This difference, however, was not statistically significant ($x^2 = 0.1$, df = 1, p = 0.8). Using the method of analysis appropriate to censored data as described by Peto *et al (loc cit)* gave a healing rate ratio of 1.12, an advantage of US over mock-US of 12%.

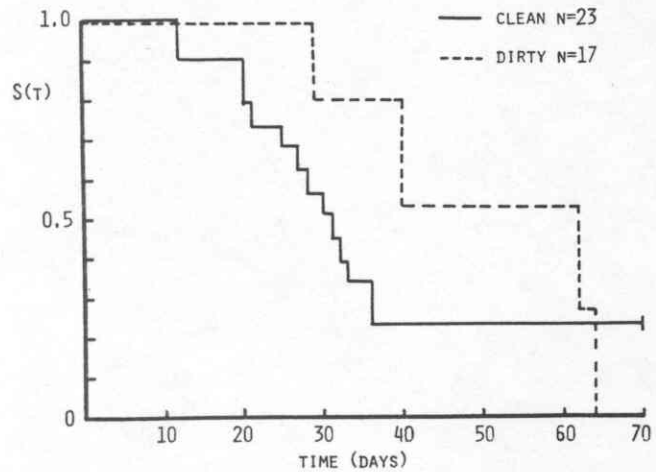

Fig 2: Life table survival curves for clinically assessed clean and infected pressure sores (S(T) is the proportion of unhealed sores)

As has been indicated earlier, there may well be many factors that influence the rate of healing of pressure sores with treatment. Figure 2 shows the healing time curves of the 40 sores divided by their initial classification as clean or infected, the corresponding median healing times being 30 and 40 days. Comparing clean to infected sores, the healing rate ratio was 2.7, suggesting that the clean sores healed nearly three times more quickly than the infected ones. This result is statistically significant ($x^2 = 4.1$, df = 1, p = 0.04) implying that a major factor influencing the healing of pressure sores is whether they are clean or infected.

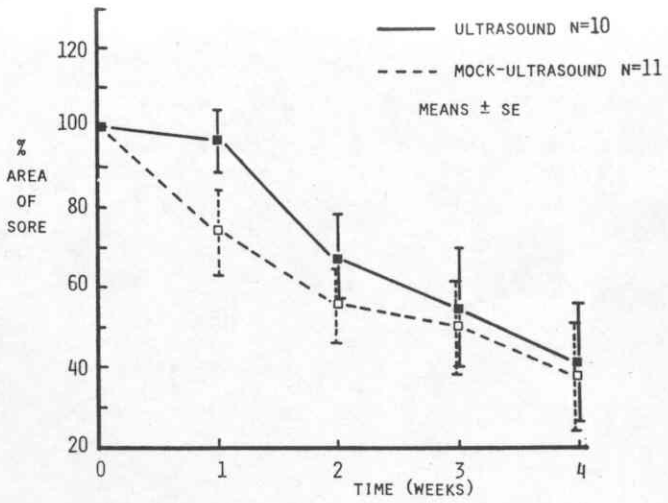

Fig 3: Graph showing average healing of clean sores in ultrasound and mock-ultrasound groups

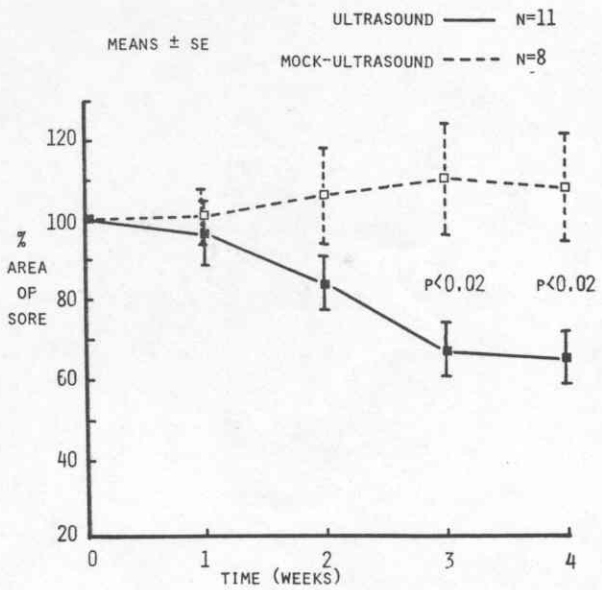

Fig 4: Graph showing average healing of infected sores in ultrasound and mock-ultrasound groups (p values: unpaired t-test)

Figures 3 and 4 show how the average healing is influenced by whether the sore has been treated with ultrasound or mock-ultrasound. From these graphs it is apparent that there is little effect of ultrasound on the healing of clean sores (unpaired t-test: week three, p = 0.8; week four, p = 0.9). There does, however, appear to be a significant effect of ultrasound on the healing of infected sores (unpaired t-test: week three, $p < 0.02$; week four, $p < 0.02$). The numbers involved here are small, so these results should be interpreted with caution. It would appear, though, that it is the infected sores, rather than the clean ones, that respond to ultrasound therapy; this suggestion deserves further detailed investigation.

Survival curves were also constructed to assess the effect of other factors which could conceivably influence the healing rate. These were the patient's age, sex, nutritional state and the Norton score, as well as the type of diagnosis, the mattress used (normal or ripple) and the size of the sore at initial diagnosis. A similar statistical analysis on each of these variables failed to show that they had any influence on the healing rate of those sores studied.

Discussion

The review of the natural history of pressure sores suggests that not only are they a very common affliction, especially in the elderly, but that there is also no satisfactory approach to their management. There is, therefore, a clear need for controlled trials to help resolve some of the controversies for it is well known that many novel treatments have a claimed benefit superior to that actually observed.

In designing the double-blind study, it was anticipated that ultrasound would double the healing rate of pressure sores. It was also assumed that patient recruitment would be sufficient to detect such a difference with reasonable statistical power. In the event, the therapeutic effect of US on all the patients taken together appears to be marginal although it is important to note that our study does not rule out a doubling of the healing rate of US over the placebo.

Whether the difference here observed is evidence of a real therapeutic effect of US or just chance variation can only be settled by a prospective randomised trial involving many hundreds of patients. For example, if the median healing time is in fact reduced by US from approximately five to four weeks (values consistent with our results and yet clinically worth while) then with a two-sided test at 5% and power of 90%, this would require approximately 850 patients to be recruited to the trial. Our experience is that patient losses may be as much as 50% so that planned recruitment to such a trial should be in the order of 1,300 patients. We believe, however, that such a trial would justify itself on the basis of the potential impact its result could make on the physiotherapeutic management of pressure sores.

The indication that ultrasound may be of specific value for patients with infected sores is of particular clinical interest and for that reason should be investigated more thoroughly in a larger population of patients. In general terms, it seems reasonable to speculate that if a clean sore is already healing at a rate near to that of its optimum biological potential (because of good wound management), then neither ultrasound nor any other additional therapy could be expected to improve its repair rate. The more slowly healing infected wound, on the other hand, offers scope for improvement by means of therapeutic intervention with the complex balance of factors which determine the healing rate. For example, infected sores are likely to contain a greater number of macrophages, and it has been speculated that ultrasound stimulates the production of wound factors from macrophages (as well as other cells) in the inflammatory phase of healing (Dyson, 1984b). Finally, this result also suggests that in a larger trial the relative insensitivity of clean sores to ultrasound therapy could mask a more marked benefit on infected sores, and therefore should be taken into account in the design of future trials.

Conclusion

From this preliminary study we have found that assessment of ultrasound therapy in a real clinical setting is possible. The treatment appears to be of marginal benefit to a general population of patients with pressure sores. A study to establish with statistical confidence that such a benefit does exist would require a trial of over 1,000 patients. There is evidence that ultrasound increases the rate of healing of pressure sores which are judged clinically to be infected.

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