960 — LOW-LEVEL PULSED RADIOFREQUENCY FIELDS AND THE TREATMENT OF SOFT-TISSUE INJURIES *

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SUMMARY

The aim of this lecture is to outline the main physiological processes involved in the heating of wounds and to suggest a mechanism by which pulsed radiofrequency (RF) energy, or the currents induced in tissues by the application of that energy, may influence its course.

Emphasis is given to the part played by oedema in inhibiting the processes of wound healing. Reference is made to the growing evidence that pulsed RF energy affects the time course of wound healing and the hypothesis is proposed that one possible mechanism by which pulsed RF energy accelerates wound healing is by reducing oedema.

INTRODUCTION

Interest in the therapeutic potential of pulsed RF energy was stimulated following reports of bioelectric fields being associated with amphibian limb regeneration and bone mechanics [1–3]. It was at about the same time the first reports of the use of pulsed electromagnetic fields in relation to wound healing emerged [4–10].

Much of the initial work, particularly in the orthopaedic applications, was performed using direct current, pulsed direct current or alternating current, but more recently similar effect on bone healing have been demonstrated using pulsed electromagnetic field [11–13]. Watson [14] has reviewed bioelectrical effects in hard tissue applications and Frank and Szeto [15] have reviewed electromagnetically enhanced soft-tissue wound healing.

It was noted by Cameron [7] that pulsed radio frequency treatment of a surgical incision in the dog resulted in less severe oedema than in the untreated controls. If pulsed RF energy reduces oedema and so accelerates the preliminary stages of wound healing, it should also enhance the second and third phases. It is this hypothesis that has been investigated.

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Types of wound healing

Wound healing is usually divided into four main types according to the type of tissue involved and the nature and treatment of the wound [16]:

(i) Primary wound healing — a soft-tissue wound closed by surgical procedure. This occurs in the vast majority of surgical wounds in which the edges of the wound are apposed.

(ii) Secondary wound healing — a soft-tissue wound left to granulate as a means of closure. This occurs in wounds in which the edges are widely separated either as a deliberate surgical policy or as a consequence of tissue loss or destruction. This type of wound healing is most often encountered in pressure sores, leg ulcers and burn injuries.

(iii) Hard tissue healing — the repair of fractures by bone regeneration. this will not be covered further.

(iv) Healing in specialised tissues — lining epithelia and nerve tissue.

Phases of wound healing

The features of wound healing involve an acute inflammatory phase, a reparative phase, and a remodelling phase [17–20]. The time span for these events to take place can be measured in minutes and hours in the first phase, days to weeks in the second, and months to years for the third and final phase, at the end of which the wound is completely healed.

These three phases of wound healing consist principally of the following physiological events:

(a) The acute inflammatory reaction phase
 (i) Changes in vascular permeability.
 (ii) Appearance of fibrin.
 (iii) Infiltration of leucocytes and macrophages.
 (iv) Localised extravasation of blood.
 (v) Alteration in histamine and local hormone levels associated with bradykinins, prostaglandins and complement.

(b) The reparative phase
 (i) Decrease in local inflammatory reaction.
 (ii) Appearance of fibroblasts in the wound area.
 (iii) Associated production of collagen by the fibroblasts leading to increased wound tensile strength.
 (iv) Absorption of extravasated blood constituents.
 (v) Epithelial migration and basal cell mitotic activity.

(c) The remodelling phase
 (i) Longer period of slower collagen deposition.
 (ii) Crosslinking of collagen fibres.

(iii) Repair of nerve endings.

(iv) Formation of scar tissue.

In secondary wound healing the following additional events occur during the reparative phase:

(i) Proliferation of capillary loops into the defect.

(ii) Formation of granulation tissue in the area of tissue loss.

(iii) Epithelial migration over the granulation tissue.

(iv) Maturation of fibrous tissue from the granulation tissue.

A disadvantageous feature of secondary wound healing is that when the granulation tissue is resorbed it converts into massive fibrous tissue which leaves a puckered scar.

Factors affecting wound healing

There are many factors which influence the course of healing; the main factors of importance are listed below [18,21–25]:

(i) Blood flow to the site of injury.

(ii) Transport of oxygen to the wound.

(iii) Oedema and inflammatory reaction in the wound.

(iv) Nutritional status (Vitamin A, B, C and D, zinc and proteins are all essential).

(v) Underlying pathologies, *e.g.* renal failure, diabetes mellitus.

(vi) The effects of some drugs, *e.g.* steroids.

Wound healing and oedema

Blood flow and hence the transport of oxygen to the wound is of paramount importance in the normal sequence of healing. Respiratory uptake of oxygen by haemoglobin in red blood cells occurs in alveoli in the lungs. It is then transported in the peripheral circulation to capillaries in the tissues. Oxygen diffuses out of the capillaries, through the interstitial spaces and into the cells. The rate of diffusion depends upon the oxygen tension gradient across the interstitial space and the overall distance between the capillaries and the cells [22,26].

Oedema is an accumulation of fluid in the interstitial spaces between the cells [27]; it is the cause of swelling and, in the case of a surgical wound, may cause visible tension around the suture line [28]. Oedema occurs during the inflammatory reaction phase of wound healing as a result of changes in microvascular permeability [29].

In Sevitt's classic work in 1958 [30] he described the cycle of events following burn injury which leads to tissue necrosis. He pointed out that oedema reduces the perfusion pressure by raising the pressure within the tissue. Oedema occludes the capillaries at the site of the wound and thereby prevents the flow of blood. This in turn reduces the supply of oxygen to the cells [31]. In addition, the accumulating oedema between the cells and the capillaries increases their physical separation

which slows oxygen diffusion from the capillaries to the cells. This view is supported by the work of Remensnyder [32] demonstrating that steep oxygen gradients exist over very short distances surrounding a 1 mm burn of the rat cremaster. Moreover, he showed that the hypoxic areas of the wounds corresponded to the observable areas of vascular stagnation and thrombus formation.

The influence of oedema is not limited to the inflammatory phase of wound healing. For example, Speer [33], using a primary wound healing model, demonstrated a significantly lower tensile strength in the portion of a wound which had been associated with relatively severe oedema. He also documented evidence that the oedematous areas of the wound showed relatively slow afferent and efferent microcirculation compared with the non-oedematous areas. It seems likely that the dynamics of the microcirculation is altered by oedema. The destructive inflammatory phase of wound healing is thus prolonged, resulting in the delayed onset of the collagen synthesis phase of wound healing [34].

This concept of a prolonged inflammatory phase of wound healing is supported by the demonstration [29] that low tissue oxygen tension (indirectly caused by oedema) may be responsible for increased capillary permeability. The existing interstitial oedema is thus further compounded.

In conclusion, oedema exerts three detrimental effects during the inflammatory phase of wound healing:

(i) Stagnation due to increased tissue tension.
(ii) Increased distance for oxygen diffusion.
(iii) Increased permeability of the capillaries.

These effects interact to delay the onset of collagen production which, in turn, delay the development of tensile strength of the wound.

TENSILE STRENGTH OF RAT ABDOMINAL WOUNDS

Introduction

The effect of pulsed RF energy on the development of tensile strength of a wound was investigated in a laboratory animal model. The purpose of this study was to compare, at two time intervals following surgery (2 days and 8 days), the tensile strength of rat abdominal wounds treated with one of two pulsed radio-frequency devices (15 W or 2 mW nominal output) compared with a placebo equivalent (15 W light bulb).

Method

110 Wistar rats (200 grams) were used in this study. Under ether anaesthesia a 2.5 cm transverse incision was made in the abdominal wall through to the peritoneal cavity of each rat. The wounds were closed with five interrupted silk sutures through all layers and the rats were randomly assigned to one of three treatment groups: 15 W, 2 mW or placebo.

The daily treatment regimen for each of the groups respectively was three episodes of 20 min exposures to the 15 W device, overnight exposure to the 2 mW device, or three episodes of 20 min exposure to the 15 W light bulb. Treatment continued until the randomised sacrifice of each animal at two or eight days post-operatively.

Prior to sacrifice each rat was anaesthetised, a plastic bag was inserted into its peritoneal cavity and its sutures were removed. The bag was progressively inflated with water at a constant rate until the wound ruptured. The pressure of water in the bag was recorded continuously to determine the resistance of the wound to increasing intra-abdominal pressure.

Device specifications

(i) Placebo device - 15 W light bulb.
(ii) 15 W pulsed RF device:

Nominal power output	15 W
Carrier frequency	27 MHz
Pulse width	65 μs
Pulse repetition frequency	200 Hz

(iii) 2 mW pulsed RF device:

Nominal power output	2 mW
Carrier frequency	3 MHz
Pulse width	100 μs
Pulse repetition frequency	1 kHz

Results

The profiles of the tracings of pressure against time were different at the two different time intervals. Two days after incision the wounds were still quite weak and there was a single point at which each wound completely broke down. Eight days after incision there was a biphasic response. A first pressure peak was reached when the fascia ruptured, allowing the bag to spread out and the water pressure to drop. A second peak was then reached when the skin itself parted.

Three separate methods were used to quantify the tensile strength of the wounds:

(i) End volume — the total volume of water infused into the bag when the wound burst. This value was extremely variable at eight days and is not reported.

(ii) Area under the graph — this integrates the time period (seconds) over which pressure of water (mm Hg) was withstood and hence allows for different sized peritoneal cavities and for differences in the extent to which the bags spread out.

(iii) Wound index (8 day groups only) — this is the sum of the two pressure peaks multiplied by the time difference (in seconds) between them.

TABLE 1

Tensile strength of rat abdominal wounds at two and eight days following transverse surgical incision

	2 DAY			8 DAY		
	value	% increase	p value	value	% increase	p value
Placebo groups						
n = 25						
End volume	97.7	–	–	–	–	–
Area under graph	1777.2	–	–	13116.4	–	–
Wound index	N/A	–	–	10563.4	–	–
15 W groups						
n = 25						
End volume	112.7	15.4	0.025	–	–	–
Area under graph	2252.2	26.7	0.025	20642.5	57.4	0.025
Wound index	N/A	–	–	17563.4	66.3	0.01
2 mW groups						
n = 5						
End volume	113.6	16.5	0.025	–	–	–
Area under graph	3256.6	83.2	0.01	13910.0	1.1	NS
Wound index	N/A	–	–	15287.0	44.7	0.01

T tests were used to compare the experimental groups with the placebo groups and the results are shown in Table 1.

Conclusions

These results clearly show that pulsed radiofrequency energy from both these devices does have a significantly effect on the tensile strength of rat abdominal wounds.

Despite the gross differences in the physical size and power output of the two devices (15 W and 2 mW), they showed a very similar profile of activity in enhancing the development of tensile strength. This confirms that the effect of pulsed radio frequency energy on wound healing is not thermal in origin.

HUMAN EXPERIMENTAL SKIN WOUNDS

Introduction

If an effect of pulsed RF energy on oedema leads to improved oxygen supply and the earlier appearances of the reparative events of the second phase of wound healing, its beneficial properties will not be confined to primary wound healing.

Two double-blind experiments were performed to determine the effect of treatment with pulsed RF fields on the histological appearance of repaired human full-thickness punch wounds of the skin of the lower limbs. This is a secondary

wound healing model which permits good experimental control. The first experiment sought to establish whether any effect of pulsed RF field could be observed.

The purpose of the second experiment was to investigate at what point in time the thickened epithelium observed in the first study developed, and to obtain histological evidence confirming that the events of the reparative phase of wound healing occur earlier in the treated wounds.

Method

Experiment 1: A full-thickness disc of skin (2 cm diameter) was removed from each inner calf of a human volunteer. Each wound was allocated an identical treatment device, one active and the other placebo. The identity of the device was revealed only when the wounds had completely healed. The devices were worn for 16 h a day until that time. Biopsies of both wounds were performed nine months after healing. The tissue was sectioned and stained with either Haematoxylyin + Eosin or Van Gieson. The sections were examined by a histopathologist who was not aware which wound had been actively treated.

Experiment 2: In this double-blind experiment, a series of twenty (3 mm diameter) full-thickness wounds were made on the upper aspect of the thighs of a human volunteer. Ten wounds received placebo treatment, the other ten received active treatment. The pulsed RF devices were similar to the lower power devices used in the rat tensile strength experiment and were worn continuously. Biopsies of the wounds were performed during the initial period of healing, at 1, 2, 3, 5, 7, and 14 days. The results shown below are a summary of all of time groups.

Device specification

Power source	3.5 V battery
Carrier frequency	44 MHz
Pulse width	100 μs
Pulse repetition frequency	1 kHz

Results

Experiment 1:

The placebo side was characterised by a thin epidermal layer (see Fig. 1, side B) and showed other features of normal secondary wound healing:

(i) Basal epidermal layer pleomorphism.
(ii) Lack of pallisading.
(iii) Endarteritis.

The placebo-treated wound took 54 days to heal.

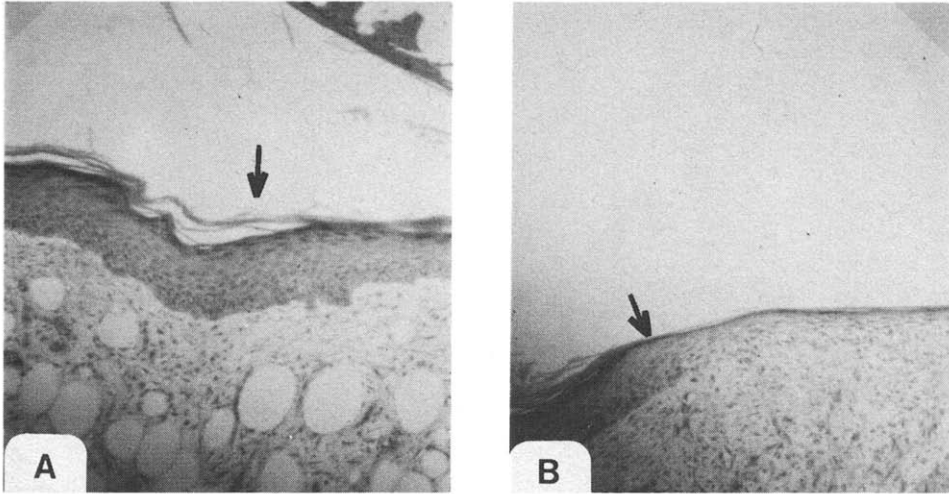In contrast, the actively treated wound showed an almost normal depth of

Fig. 1. Epidermal layer of repaired human punch skin wound. (A) Actively treated wound; (B) placebo-treated wound. (Arrows indicate the wound edges.)

epidermal layer (see Fig. 1, side A) and other advantageous features not usually associated with secondary wound healing:

(i) No pleomorphin.

(ii) Basal cell pallisading.

(iii) No endarteritis, but developed endothelium.

The actively treated wound took 39 days to heal.

Experiment 2:

As with the first experiment the placebo-treated wounds showed the typical features of secondary wound healing:

(i) Thin epidermia.

(ii) Basal-layer pleomorphism.

The actively treated wounds showed evidence of:

(i) Earlier epidermal budding.

(ii) Earlier migration into the wound.

(iii) Earlier appearance of rete ridges.

(iv) Almost normal depth of final epidermis.

Conclusions

Treatment of skin wounds with pulsed radio-frequency energy influenced the processes of acute secondary wound healing. The rate of healing was accelerated and the histological appearance of the actively treated wounds showed that the

healed epidermis was more like normal skin than the scar tissue typical of secondary wound healing.

MENINGOMYELOCELE STUDY

Introduction

A meningomyelocele is a hernial protrusion of the meninges and spinal cord roots through a bony defect in the vertebral column. Some infants are born with this condition, requiring surgical closure of the defect within the first few days of life. One of the complications of the procedure is dehiscence of the wound (due to the tension of the skin across the operative site). The meninges may become exposed, thus providing a route for infection which may lead to ascending meningitis. This can end in mortality.

The purpose of this study was to determine the effects of pulsed RF energy on the integrity of surgical closure of this defect. If treatment with pulsed RF fields leads to a reduction in oedema then tissue tension would be lower and there would be a reduced likelihood of the wounds breaking down.

Method

A prospective study was started in 1974. It ran for seven years and involved 90 patients. The surgical procedure was performed by the same surgeons throughout the duration of the study. This study was not double-blind, a retrospective study of the previous 470 cases performed in the unit confirmed a wound breakdown rate of 7%. The pulsed RF devices were placed over the wound dressings post-operatively and treatment lasted for 16 h a day until four weeks after surgery.

Written assessments of all the wounds were completed daily and photographic confirmation of the post-operative course of some wounds was collected by ward staff. Neurological status was assessed by physiotherapists before and after surgery and at regular intervals thereafter.

Device Specifications

Specifications for the device used in this study are not available.

Results

In the first 90 patients entered into the study, the incidence of wound breakdown was significantly reduced from 7% to 0% ($\chi^2 = 6.67$, $p = 0.01$).

Conclusions

Wound breakdown following meningomyelocele closure with its attendant risk of scending meningitis was eliminated. There were no obvious alterations in surgical

technique or in post-operative care that might have accounted for the reduction in wound breakdown.

These results suggest a considerable benefit to be derived from treatment with pulsed RF energy and clearly warrant further investigations under double-blind conditions.

BLEPHAROPLASTY STUDY

Introduction

The surgical procedure of blepharoplasty may be performed under general or local anaesthesia and involves removal of excess skin and fat from the upper and/or lower eyelids. The low tension in the skin of the peri-orbital region means that post-operative oedema and bruising are inevitable. It is an ideal clinical model for double-blind evaluation of pulsed RF treatment because it provides asymptomatic patients who each undergo a bilateral procedure performed by a single surgeon; the patient acts as his or her own control.

A double-blind pilot study has been reported previously [35]. In the pilot study no attempt was made to obtain any numerical estimates of oedema and bruising on which to perform statistical analysis. The purpose of the present study was to replicate the clinical effect observed in the pilot study and to quantify that effect using a larger sample of patients.

Method

The subjects of this clinical study were the patients of a plastic surgeon (Mr. F.V. Nicolle) practising in London, England. All patients attending for bilateral blepharoplasty who gave their informed consent to participation were entered into the study; there were no specific exclusion criteria. Patients receiving surgery to the upper lids and/or the lower lids were included.

Patients were randomly assigned a pair of special lensless spectacles to provide treatment to the lids of one eye but not the other. Active and placebo antennae were fitted into the light weight spectacle frames and electrical components were housed in one leg of the frames. The placebo antenna was electrically shielded to prevent re-radiation from the active antenna which emitted pulsed RF energy of the following specifications:

Nominal power output	73 μW
Carrier frequency	26 MHz
Pulse width	73 μs
Pulse repetition frequency	900 Hz

Patients therefore acted as their own control and they were not aware which eye received treatment. Treatment commenced immediately following surgery and the patients were instructed to wear the spectacles for 16 h per day for the following

three days. Apart from this no modifications were made to the normal post-operative care of the patients. Patients were asked to keep a log, on a small card provided, of the hours for which they wore the spectacles.

At each post-operative visit, that is at one day (a few cases only) and at three, four of five days after surgery, the nurse took a clinical photograph which was developed into a colour slide. The clinical logistics of the study precluded the taking of absolutely standard photographs. Therefore, in order to be able to make a correction to the measurements for the absolute size of each photograph, it was decided to place a centimetre scale reference sticker on the forehead of each patient prior to the clinical photograph being taken. Unfortunately this decision was not taken until after the first twelve patients had been entered into the study.

Measurements

The slides were used to obtain measurements of bruising and the amount each eye was open and they were also clinically assessed by a panel of three judges (one surgeon, one nurse and one lay person).

The bruising beneath each eye was recorded by projecting the slide onto a piece of acetate film and then drawing a planimetric trace of the bruised regions below the median palpebral tissue on each side. Only the areas of clearly defined red or purple bruising were included, not the rather diffuse areas of yellow. A System III Image Analysis Machine (AMS Limited) was then used to measure the area (in square centimetres) of the planimetric trace beneath each eye.

The slides were then projected onto a white piece of paper on which two thin black " + " signs had been drawn. The height of the palpebral fissure of each eye (at the point of bisection of the pupil) and the size of the centimetre scale reference sticker (when present) were marked off on the " + " signs with a thin pencil. The paper was then laid flat to enable the amount each eye was open and the length of the scale reference sticker to be measured with a ruler.

To obtain ratings of the extent of oedema, bruising and scleral haemorrhage, the three assessors examined the projected slides and recorded a rating of each clinical sign on a specially prepared form. The eyes were rated on the following scale for each sign:

2R The patient's RIGHT eye shows *significantly less* $- - - - -$ than the patient's LEFT eye.

1R The patient's RIGHT eye shows less $- - - - -$ than the patient's LEFT eye but this is of *little clinical significance*.

0 There is no discernable difference between the patient's LEFT and RIGHT eyes with respect to $- - - - -$.

2L The patient's LEFT eye shows *significantly less* $- - - - -$ than the patient's RIGHT eye.

1L The patient's LEFT eye shows less $- - - - -$ than the patient's RIGHT eye but this is of *little clinical significance*.

All of the Day 3 (4 or 5) photographs were assessed before any of the Day 1

photographs and the three assessors were blind as to the side of treatment of each patient.

Analyses

Bruising and eye-opening data were analysed using related samples t tests and contingency tables were drawn up of the clinical assessment data and submitted to χ^2 tests of association.

Patients who failed to return the log of the times the spectacles had been worn or who wore the spectacles for fewer than 8 h per day for at least two days were excluded from the analysis.

Because not all of the pictures were taken with the patients wearing a scale reference sticker it was not possible to provide a correction factor to the measurement data in every case. Two analyses were therefore performed. To include all patients, the data was transformed to the percentage of total bruising or eye opening
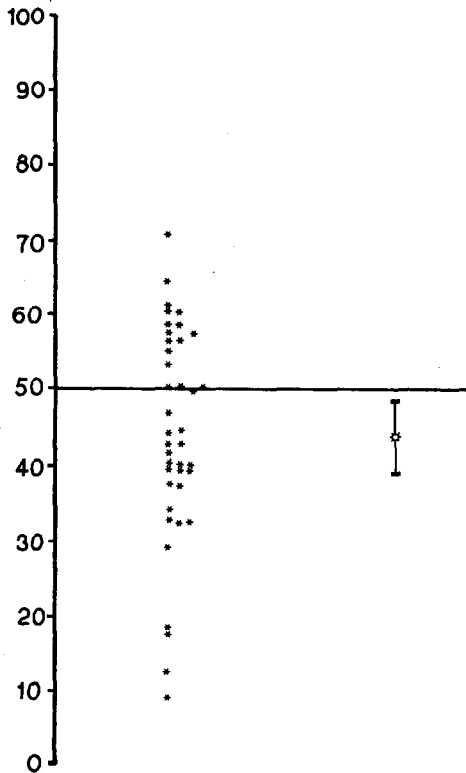

Fig. 2. Percentage of total bruising which was on the active side (Day 3, 4 or 5 post-operatively). Graph shows individual score for each patient and the group mean (± 95% confidence intervals).

which was on the active side. The second analysis, which used the measured size of the scale reference sticker to convert the bruising data to actual areas, is considered to give a more meaningful picture even though it included fewer patients.

Results

There were a total of sixty patients available for analysis in the present study. Two of these patients failed to return the log of the times when the spectacles were worn, two had worn the spectacles for fewer than the required 2 days and fourteen had worn the spectacles for fewer than the required 8 h per day. There were thus forty-two patients entered into the analyses, of whom nine patients had slides from Day 1 Post-operation and of these two had slides from Day 1 only.

Figure 2 shows the area of bruising on the actively treated side as a percentage of the total bruising of both sides. It can be seen that for the patients as a whole the percentage of the total bruising which was on the ative side was significantly less
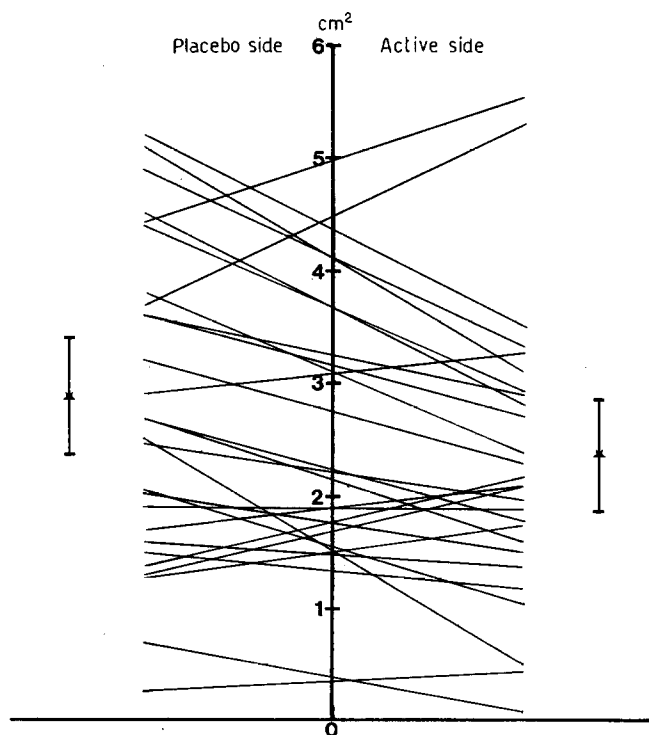

Fig. 3. Actual areas of bruising on the actively treated side and the placebo side (Day 3, 4 or 5 post-operatively). Graph shows the scores for each patient and the group means (±95% confidence intervals).

than 50%, which is the outcome which would be expected to occur by chance ($t = 2.56$, $p = 0.015$). This is equivalent to a mean reduction in bruising on the active side of 20.7% (95% confidence interval, 5.2% to 33.8%).

For the 28 patients who had worn the scale reference sticker it was possible to convert the bruised area measurements to actual areas. Figure 3 shows these results. It can be seen that the mean area of bruising on the placebo side was 2.88 cm^2 and for the active side it was 2.38 cm^2. This difference was again statistically significant ($t = 2.47$, $p = 0.02$) and indicates that there was 17.4% less bruising on the actively treated side (95% confidence interval, 3.7% to 31%).

Figures 4 and 5 show, for the Day 1 and Day 3, 4 or 5 photographs respectively, the height of the palpebral fissure of the actively treated side as a percentage of the
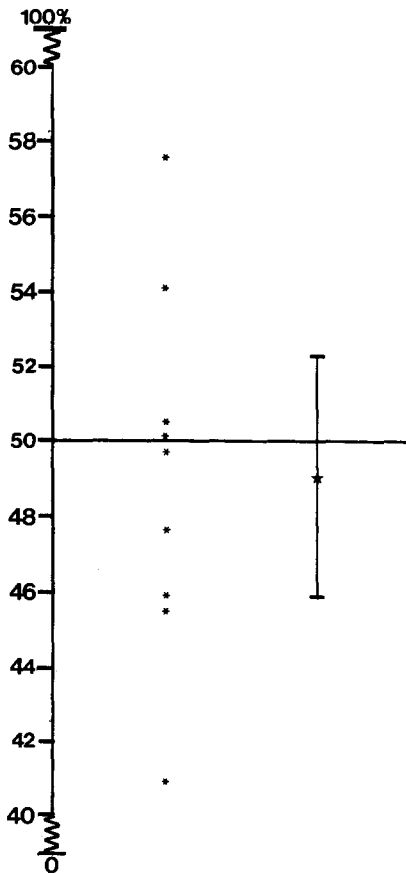

Fig. 4. Height of the palpebral fissure on the active side as a percentage of the combined height of the fissure of both eyes (Day 1 post-operatively). Graph shows individual score for each patient and the group mean ($\pm$95% confidence intervals).
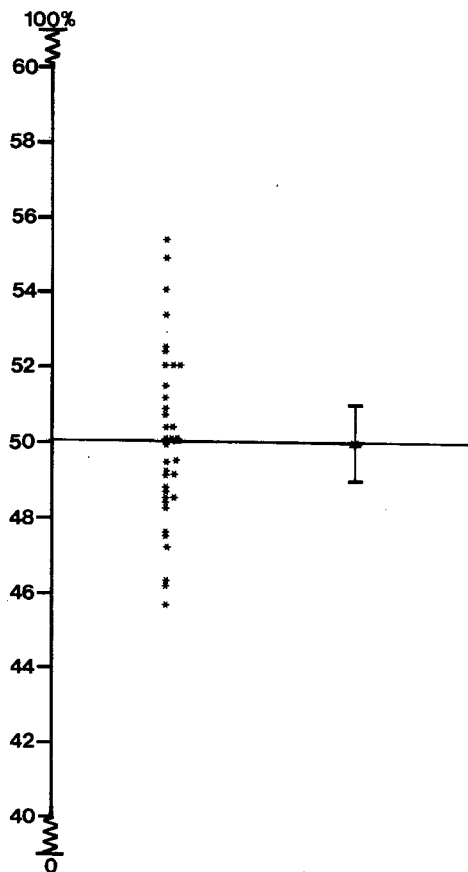
Fig. 5. Height of the palpebral fissure on the active side as a percentage of the combined height of the fissure of both eyes (Day 3, 4 or 5 post-operatively). Graph shows individual score for each patient and the group mean ($\pm 95\%$ confidence intervals).

combined heights of the palpebral fissures of both sides. In neither case is this value significantly different from 50% (Day 1: $t = 0.52$, NS; Day 3, 4 or 5: $t = 0.62$, NS).

Although the clinical sign of oedema is more striking on the first day following surgery, too few patients with Day 1 photographs were available to permit a meaningful analysis of the clinical assessments of them. Even for the Day 3, 4 or 5 photographs there were not sufficient patients to perform a reliable analysis of the full five assessment levels. However, by combining the two levels of assessment on each side (2R and 1R, and 2L and 1L) and excluding the small number of cases assessed as showing no difference, the cell entries are large enough to permit meaningful conclusions (see Table 2). It can be seen that there is a strong

TABLE 2

Clinical assessment of oedema by surgeon assessor (Table combining assessment levels)

	Less oedema on left	Less oedema on right	Total
Left side active	12	5	17
Right side active	5	13	18
Total	17	18	35
Statistic	Value	D.F.	Probability
Pearson χ^2	6.4	1	0.01

association between the clinical assessments made and the side of activity of the spectacles that the patient was wearing (Pearson $\chi^2 = 6.4$, $p = 0.01$).

Table 3 similarly shows the same surgeon's assessments of the patients' bruising. Again the association between assessments made and side of activity of the spectacles worn is statistically significant (Pearson $\chi^2 = 5.9$, $p = 0.015$).

Only six patients show any scleral haemorrhage and there is no evidence of its presence being associated with the side of activity of the spectacles being worn (Pearson $\chi^2 = 1.3$, NS).

The results of the other two assessors were in broad agreement with the findings of the surgeon, though, with more assessments being recorded as *no discernable difference*, the same levels of significance were not attained.

Discussion

The results of the present study provide objective evidence for and statistical underpinning of the clinical impressions reported in the pilot study. After approximately three days of post-operative treatment with low levels of pulsed RF energy there is a clear reduction in the area of bruising and in the observable signs of oedema around the treated eye in comparison with the untreated eye.

TABLE 3

Clinical assessment of bruising by surgeon assessor (Table combining assessment levels)

	Less bruising on left	Less bruising on right	Total
Left side active	12	4	16
Right side active	6	12	18
Total	18	16	34
Statistic	Value	D.F.	Probability
Pearson χ^2	5.9	1	0.015

GENERAL DISCUSSION

Four studies have been described which provide support, from both laboratory and clinical research environments, for the contention that pulsed RF fields may be of value in the treatment of soft tissue-injuries. Furthermore, the hypothesis that such effects may be mediated through a reduction in oedema has been upheld. As argued in the introduction, the influence of oedema, which occurs during the inflammatory reaction phase of wound healing, may extend beyond this phase and result in lower wound tensile strength and delay the onset of collagen synthesis [34]. The laboratory study of rat abdominal wound repair has indeed demonstrated that tensile strength is more developed in the groups treated with pulsed RF energy. Further evidence that the physiological events of the reparative phase of wound healing occur earlier following treatment with pulsed RF fields was found in the human skin wound experiments; the first experiment showed an improved end result and in the second experiment histological evidence of repair appeared earlier in the treated wounds. That these effects were not confined to the laboratory setting was demonstrated in the meningomyelocele study in which wound breakdown following surgery was eliminated. This might have been due to improved tensile strength of the wound or to a reduction in oedema creating a lower bursting pressure (or both), although it must be stressed that this was not a randomized control trial. Finally, in the blepharoplasty study direct evidence has been obtained that pulsed RF treatment reduces both bruising and oedema. Oedema is produced by changes in microvascular permeability, by the breakdown of extravasated proteins (which increases tissue osmotic pressure), by increased capillary blood pressure and by increased fluidity of the tissue ground substance (preventing the rise in tissue tension which opposes further release of exudate) [25]. One possible mechanism of action of the pulsed RF fields might be to prevent the disaggregation of the mucopolysaccharides of ground substance which causes its increased fluidity and is one of the earliest features of the inflammatory response. In this way the fluid exudate and free red blood cells from the damaged capillaries would be less able to spread from the initial site of injury. It is interesting in this context to note that attempts to model the effects of electric fields on connective tissue [36] have concentrated on the polysaccharides (GAGs) which are the main charge-bearing constituents.

CONCLUSIONS

The body of research into the effects of treatment of wounds with pulsed RF fields has demonstrated:
(i) Earlier appearance of tensile strength.
(ii) Evidence of earlier onset of reparative processes in secondary wound healing.
(iii) Reduced bruising and oedema is primary wound healing.
It may therefore be concluded that treatment with pulsed RF or similarly configured devices can accelerate some processes of primary and secondary wound

healing. It is not proven that these effects are mediated through a reduction of interstitial oedema; there may be a number of separate mechanisms involved.

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