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Successful Use of Low-intensity Pulsed Ultrasound in the Rescue of Failed Vascularised Fibular Graft for Radial Non-union

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Authors' contributions

This work was carried out in collaboration between both authors. The both authors jointly designed, analyzed and interpreted and prepared the manuscript. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

We present the case of a 47-year-old man who developed a non-union of the left radius following an open double barrel fracture to the left forearm sustained in a road traffic accident. Whilst initially treated with internal fixation, only the ulna fracture united. The patient then underwent two failed radial non-union revision surgeries with exchange of plate and simple bone grafting. A third attempt to rescue the non-union was made with a vascularised bone graft, using a composite fibula/skin free flap. However, within one week the vascular anastomosis failed, and the whole free flap, except the no longer vascularised fibular graft, was excised. Given the previous surgical failures, adjunctive use of low-intensity pulsed ultrasound treatment was started and led to union 6 months later. We report that as an adjunct to union low-intensity pulsed ultrasound treatment can succeed where multiple previous bone grafts alone for non-unions failed, including a vascularised bone graft in which its vascular anastomosis was subsequently compromised.

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1. INTRODUCTION

Sometimes fractures do not heal in the normal time expected given the location, and degree of displacement and comminution of the fracture, as well other patient factors including age and smoking status. When significant time has elapsed such that the fracture is no longer expected to heal, a non-union has occurred [1]. Given the many variables involved in defining when a non-union has occurred, no absolute time-based definition exists but they are typically diagnosed 6-9 months after the initial injury if no union has occurred.

Non-unions of long bones such as the radius are typically initially managed surgically with internal fixation using compression plates. This is often accompanied by non-vascularised bone grafting [2]. If these measures fail to induce union, other surgical options may be required. These include distraction osteogenesis in which the Ilizarov apparatus provides stable fixation and controlled interfragmentary compression and distraction to stimulate callus formation. This procedure is particularly indicated for hypertrophic non-unions [3]. An alternative 'last-line' surgical option, especially when the vascularity of the non-union site is believed to be compromised, is vascular bone grafting. This is attempted before amputation is considered for symptomatic improvement of the patient's pain [4].

The rationale for vascularized bone grafting follows the premise that an adequate blood supply to the site of the fracture is needed to facilitate ossification in bone healing [5]. Unfortunately, the more surgical procedures a patient undergoes, the more the patient's local blood supply becomes damaged and the more fibrous scar tissue forms, which too can compromise fracture healing by preventing a front of new blood vessels and osteoblasts from reach the fracture site [6]. However, vascularized bone grafting is not without its complications – a comparison of vascular versus non-vascularized fibular autografting in 53 patients for the repair of long diaphyseal defects following primary sarcoma resection found that vascularized bone grafting was associated with significantly shorter complication free survival time (36 months vs. 88 months in the non-vascularized fibular autograft treatment arm). These subsequently required more surgical revisions, with indications including the development of non-union [7].

Given the invasive nature of procedures such as vascularized bone grafts, alternative non-invasive methods of stimulating bone healing in non-unions have been sought. One such option has been the use of low-intensity pulsed ultrasound devices in treatment. These high-frequency acoustic pressure waves can be mechanical stimuli to living tissues, resulting in downstream changes in transcription factor expression, which may promote tissue healing [8]. Its use in rat femoral fractures has demonstrated that the treatment accelerates healing, with increased endochondral ossification, bone bridging and bone remodeling with corresponding increases in torsional torque and stiffness of the healed bones compared to controls [9]. *In vitro* studies have suggested the sub-cellular mechanisms mediating this improved bone healing may include stimulation of osteogenic transcription factor expression, including Runx2 [10] and osteonectin and osteopontin [11]. Furthermore treatment increased osteogenic differentiation of mesenchymal stem cells, [10] activated osteogenic activity in periosteal cells and increased the expression of vascular endothelial growth factor in a dose-dependent fashion in cultured periosteal cells, consistent with the notion that low-intensity pulsed ultrasound treatment facilitates angiogenesis necessary for fracture healing [12].

Significant clinical evidence already exists to demonstrate the utility of low-intensity pulsed ultrasound in the treatment of non-unions and delayed unions. Nolte et al. [13] demonstrated an 86% success rate of low-intensity pulsed ultrasound in established non-unions. Roussignol et al. [14] performed a retrospective study of 59 patients with non-union, finding an 88% consolidation rate at 6 months. Schofer et al. [15] performed a multi-centre randomized sham-controlled trial, demonstrating significant increases in bone mineral density and significantly reduced gap area on CT scans in delayed unions after 16 weeks of treatment with low-intensity pulsed ultrasound treatment compared to sham treatment. However, there are no studies at present that have reported its successful use after a failed vascularized bone graft, usually performed after successive operative failures to induce union, which as detailed above, further compromise fracture healing potential. Our aim for this case report is to demonstrate that low-intensity pulsed ultrasound devices should be more widely and readily used in the treatment of stable non-unions. Indeed this case specifically suggests that even after previously failed non-vascularised bone grafts and a failed vascularised fibula graft in the treatment of non-union, adjuvant ultrasound treatment can result in achieving bony union.

2. PRESENTATION OF CASE

A 47-year-old male non-smoker initially presented to A&E following a road traffic accident, as a cyclist colliding with a car. The patient sustained superficial facial injuries and had an obvious left forearm deformity. Based on the clinical suspicion of an open fracture to the left forearm, standard initial management with splinting, covering the wound with a sterile dressing and tetanus and antibiotic prophylaxis was carried out. Based on clinical examination and plain radiographs taken that day (Fig. 1), the patient was found to have sustained an open double barrel fracture to the left forearm – mid-shaft fractures to the radius and ulna – as well as radiocapitellar dislocation. Initial attempts at closed reduction failed to reduce the fractures. As a result the patient subsequently underwent debridement, open reduction and internal plate fixation of the ulnar and radial fractures, with closed reduction of the radiocapitellar joint, the following day (Fig. 1).

Fig. 1. Plain radiograph taken after the initial traumatic injury. Left: showing the mid-shaft comminuted ulna fracture and mid-shaft radius fracture, with evidence of radiocapitellar dislocation before fixation. Right: post-operative, showing reduced and internally fixed radial and ulnar fractures and the now congruent radiocapitellar joint

In a follow up clinic 3.5 months later the patient was clinically found to have full range of motion (ROM) in elbow flexion and extension, full supination, but limited pronation. Plain radiographs taken that day demonstrated the fracture to the ulna had united, but the radial fracture remained un-united (Fig. 2). As the radius continued to remain un-united at 6 months following the initial injury, a diagnosis of radial non-union was then given, and as such iliac crest bone grafting and revision internal fixation was performed with the hope of inducing union. However, union did not occur and three months later revision bone grafting was performed to the patient's left radial non-union with iliac crest bone grafting and exchange of plate fixation (Fig. 3). Follow-up plain radiographs taken 4.5 months after this revision surgery demonstrated no union either side of the bone graft (Fig. 3).

Fig. 2. Plain radiograph taken at 3.5 months post-operative follow-up demonstrates the internal fixation of the ulnar fracture, which has now practically united, compared with the fixed radial fracture with plates and screws, which is un-united

After consultation with the patient regarding further surgical management options such as debridement of the radial non-union site and an ulnar shortening osteotomy, as well as fibular vascular bone grafting, a non-invasive management option of immobilization of the forearm in a cast and the use of low-intensity pulsed ultrasound treatment was chosen. A portal was created in the cast to allow the patient to self-administer the low-intensity pulsed ultrasound treatment to the non-union site with the use of an Exogen device. CT scans taken 9 months after initially starting the low-intensity pulsed ultrasound treatment showed the radial non-union of the distal side of the bone graft to be persisting (Fig. 4).

Fig. 3. Plain radiographs demonstrate the 2nd revision surgery with iliac crest bone graft and exchange of plate fixation. Left: taken post-operatively on the day of surgery. Right: taken at 4.5 month post-operatively, demonstrating the persistent radial non-union

Fig. 4. CT scans taken 9 months after initially starting the low-intensity pulsed ultrasound treatment showed the radial non-union of the distal side of the bone graft to be persisting

As a result of the persisting non-union 9 months after beginning low-intensity pulsed ultrasound treatment, a free flap fibular vascular bone graft was attempted, with the fibula longitudinally fixed over the non-union site with screws in lieu of a plate, after freshening the opposing sides of the grafted fibula and recipient radius. Unfortunately, within one week the grafted vascular anastomosis failed, evidenced by necrosis of the soft tissues and skin of the free flap. As such, the whole free flap except the now non-vascularised fibula bone graft was excised.

Given this failure, a second low-intensity pulsed ultrasound treatment cycle was started in the hope that the addition stimulation of bone healing could rescue this failed vascular bone graft. The patient was using a removable brace for forearm support and the patient began using an Exogen device post-operatively. The device was worn like a wristwatch and placed over the non-union site for 20 minutes every day during the subsequent 9 month treatment period. The ultrasound characteristics of this second treatment cycle were identical to that of the first cycle, with the device applying a 1.5 MHz frequency ultrasound wave (modulating signal burst width of 200 μs, repetition rate 1kHz) with a temporal average power of 117mW to a therapeutic Effective Radiation Area (ERA) of 3.88cm^2 to give a spatial average temporal average intensity of 30 mW/cm^2.

CT scans taken 9 months after restarting Exogen treatment following the failed free fibula vascularized bone graft demonstrated complete union of the patient's left radial mid-shaft fracture (Fig. 5). The patient was therefore recommended to stop using the brace and Exogen device, and to begin mobilizing and strengthening exercises for the whole left upper extremity.

3. DISCUSSION

In this case, a vascular bone graft was performed after several previous surgical failures of internal fixation, with non-vascularised bone grafting initially, and its subsequent surgical revisions to achieve union after an initial open mid-shaft radial fracture. The more surgical procedures a patient undergoes, the more the patient's local blood supply is compromised and the more fibrous scar tissue forms, which too can compromise fracture healing by preventing a front of new blood vessels and osteoblasts to reach the fracture site [6]. It is for this reason that vascularized bone grafting is often attempted after previous failures of non-vascularised bone grafting, with the hope of improving the vascularity of the fracture site itself. However, vascularity of the graft in this case was lost, evidenced by the subsequent necrosis of the grafted soft tissues. In any event, vascularised bone grafts may have associated post-operative complications [7], perhaps owing in part to the technical challenges presented by the involved microsurgical techniques.

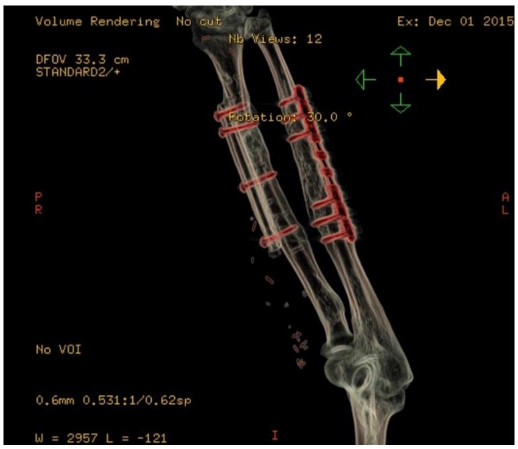

Fig. 5. 01.12.15 – CT scan 6 months after starting 2nd low-intensity pulsed ultrasound treatment cycle post-operatively, following the failure of the vascular anastomosis of the fibular vascular bone graft. Union of the patient's radius via the non-vascularised fibular graft, circumventing the radial non-union is seen

Previously, we have reported a case in which a 5-year-long ulnar non-union was stimulated to unite by the use of low-intensity pulsed ultrasound treatment as an alternative to vascularized bone grafting [16]. In this case, however, the initial round of ultrasound treatment before the vascularized bone graft was attempted was unable to stimulate the non-union to fully unite – whilst osseous bridging occurred at the proximal side of the non-vascular bone graft, the distal side of the graft did not, presumably due to a poorer blood supply in that area. Here, in an attempt to circumvent the site of non-union that was otherwise stable, bridged by fibrous tissue, the opposing longitudinal sides of the fibula bone graft and the radius to which it was fixed were refreshened.

Whilst this process may have further degraded the vascularity of the area surrounding the non-union given the eventual vascular compromise of the graft, the combination of increasing the surface area available for osteoblastic migration and activity by longitudinal, as opposed to cross-sectional, apposition of the refreshened sides of the graft and and radius, along with the use of low-intensity pulsed ultrasound, allowed the the non-union site to be circumvented, achieving union via the longitudinal apposition of the graft on the radius.

It may indeed be possible that this surgical technique of longitudinal apposition of the graft on the radius may have been sufficient alone to achieve union. However, given the several previous operative failures of non-vascularised bone grafts in this patient, we believe without additional stimulation this would be unlikely.

4. CONCLUSION

This case report represents the first case in which low-intensity pulsed ultrasound treatment has been used successfully to achieve bone union after the surgical failure of a vascularized bone graft in a 3-year-old post traumatic radial non-union. Our patient had also previously undergone two failed non-vascularized bone grafts to treat this non-union. This case report adds to growing body of clinical evidence regarding its efficacy in the treatment of non-unions [13-15] and goes further to suggest that its efficacy is retained even in the context of the failure of a previous vascular bone graft to treat the non-union. This effect is postulated to occur by the pulsed ultrasound waves to act as a mechanical stimulus at the non-union site, resulting in the activation and expression of osteogenic transcription factors including Runx2 [10], osteonectin and osteopontin [11], increasing osteogenic differentiation of mesenchymal stem cells [10] and increasing the expression of vascular endothelial growth factor [12], thereby promoting bone healing at multiple stages to aid in achieving union. This is evidenced by the success of low-intensity pulsed ultrasound in this case report in achieving union, even when the vascularity of the fibular vascular bone graft itself was lost, requiring excision of the necrotic skin and soft tissues of the free flap.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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