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● *Original Contribution*

LOW-INTENSITY PULSED ULTRASOUND THERAPY STIMULATES CALLUS FORMATION BETWEEN HOST FEMUR AND CORTICAL ONLAY STRUT ALLOGRAFT

Haruhiko Akiyama,[*] Yudo Hachiya,[†] Hiromi Otsuka,[‡] Makoto Kurisuno,[‡] Keiichi Kawanabe,[*§] Naoyuki Katayama,[||] Hisanori Ohura,[||] Koji Yamamoto,[*] Keiji Sato,[‡] and Shuichi Matsuda[*]

[*]Department of Orthopaedics, Kyoto University, Kyoto, Kyoto, Japan; [†]Hachiya Orthopedics, Nagoya, Aichi, Japan; [‡]Department of Orthopaedic Surgery, Aichi Medical University, Nagakute, Aichi, Japan; [§]Department of Orthopaedic Surgery, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan; and [||]Department of Orthopedic Surgery, Hokkaido Orthopedic Memorial Hospital, Sapporo, Japan

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Abstract—Cortical onlay strut allografting is a promising surgical option to reconstruct and reinforce the deficient femur in a hip arthroplasty. However, the union of the allograft to the host bone takes a long time. To accelerate the process of cortical onlay strut allograft healing, we studied the effects of low-intensity pulsed ultrasound (LIPUS) on callus formation. From 2 wk after the operation, LIPUS was given for 20 min/d at each end of the strut allograft. The LIPUS treatment group was assigned 14 allograft transplantations, while 21 control patients were treated without LIPUS. The LIPUS treatment group formed calluses and had complete bridging between the host femur and the allograft faster after operation (16.9 and 29.4 wk after operation, respectively) compared with the control group (40.7 and 82.0 wk after operation, respectively). Our findings showed that LIPUS stimulated bone bonding between the host femur and the cortical onlay strut allografts. (E-mail: hakiyama@kuhp.kyoto-u.ac.jp) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Hip arthroplasty, Femur, Bone, Ultrasound stimulation, Strut bone allograft.**

INTRODUCTION

The treatment of patients with bone loss, fracture or nonunion of the femoral shaft after total hip arthroplasty (THA) remains challenging. Several surgical options, including megaprosthesis (Parvizi and Sim 2004), bone substitutes (De Long et al. 2007), impaction bone grafting (Gie et al. 1993) and onlay biological plate (Emerson et al. 1992) have been developed to reconstruct and reinforce the femoral shaft. Onlay biological plates have the biomechanical advantage of giving immediate structural support at the bone loss or fracture site. Onlay autografting using fibula bone augmented with autogenous cancellous bone grafts is considered a gold standard procedure to enhance new bone formation, restore bone stock and increase cortical strength by extracortical bridging. However, the size and amount of autogenous bones and the morbidity of the donor site limit the wider application of this technique. Therefore, the use of a strut allograft is an attractive alternative to an onlay bone autograft (Emerson et al. 1992).

Previous studies showed that cortical onlay strut allografting used in conjunction with hip arthroplasty achieved good clinical and radiologic results (Barden et al. 2001; Haddad et al. 2002). Cortical onlay strut allografts unite to the host bone through callus formation, which is expected to recapitulate a process of fracture healing (Emerson et al. 1992). However, the bone incorporation of allografts progresses slowly and it takes longer to complete the union to the host bone compared with fracture healing (Emerson et al. 1992; Enneking et al. 2001). In addition, cortical allografts are strong initially, but the repair process weakens them, leading to fatigue fractures (Enneking and Campanacci 1975). These findings result in the extension of the time of protected weight bearing for the patients, thus limiting daily activity. Therefore, improving allograft union and incorporation is important for achieving a successful reconstruction and a good clinical outcome.

Low-intensity pulsed ultrasound (LIPUS) is an exogenous biophysical stimulus to accelerate a process

Address correspondence to: Haruhiko Akiyama, 54 Kawahara-cho, Shogoin, Sakyo, Kyoto 66–8507, Japan. E-mail: hakiyama@kuhp.kyoto-u.ac.jp

of fresh fracture healing through stimulation of osteogenesis, chondrogenesis, and angiogenesis. Duarte (1983) and Dyson (1983) were the first to apply LIPUS clinically for stimulation of bone formation. Pilla et al. (1990) showed that application of LIPUS for 20 min/d accelerated the recovery of torsional strength and stiffness significantly in rabbit fracture models. In a multi-center randomized double-blind placebo-controlled clinical trial, Heckman et al. (1994) demonstrated a significant reduction in the time of clinical and radiographic healings of tibia fractures.

Based on these findings, The Food and Drug Administration in the United States approved the use of LIPUS for the accelerated healing of fresh fractures in 1994 and for the treatment of established non-unions in 2000. Currently, a study has shown that daily LIPUS stimulation of the host-allograft junctions resulted in a 30% increase in reconstruction stiffness, paralleled by significant increases in callus maturity and periosteal bridging across the host-allograft interfaces in sheep (Santoni et al. 2008). However, there has been no evidence for the effectiveness of LIPUS on the healing of the cortical onlay strut allograft in humans. Therefore, we analyzed the potential of daily LIPUS stimulation of the host-allograft bone junctions in conjunction with hip arthroplasty.

MATERIALS AND METHODS

Between November 2000 and May 2011, we reviewed 35 patients (35 hips) retrospectively that had undergone primary or revision THA with cortical onlay strut allografts for femoral reconstruction (Table 1). The patients were assigned to the LIPUS treatment group ($n = 14$) or to the control group ($n = 21$). The LIPUS treatment group consisted of 2 men and 12 women, with a mean age at the time of operation of 63 y (range: 23–79 y), a height of 150.5 $\pm$ 7.0 cm and a weight of 49.8 $\pm$ 9.2 kg. The control group consisted of 4 men and 17 women, with a mean age at the time of operation of 65.8 y (range: 45–84 y), a height of 151.7 $\pm$ 9.0 cm and a weight of 52.5 $\pm$ 11 kg.

The operations were performed with an anterolateral or a posterior approach. The acetabular component and the femoral component were replaced if necessary. Cortical onlay strut allografts produced from the tibia or the femur were processed as described previously (Hachiya et al. 1999) and were preserved aseptically in liquid nitrogen. Excessive debridement of the soft tissue was avoided to preserve periosteal circulation. The endosteal surface of the allograft strut was contoured to match the outer diameter of the host femur, and the interfaces were augmented with ‘mashed’ cancellous bone allograft generated from the resected femoral head by an acetabular reamer (Fig. 1a, b, and c). One to three struts were fixed to the host femur by metallic cables or cables with metallic plates and metallic mesh (Fig. 1d).

Patients in the LIPUS treatment group were provided with the Sonic Accelerated Fracture Healing System (Smith & Nephew, Memphis, TN, USA; Teijin Pharma., Tokyo, Japan) (Fig. 2). The ultrasound signal had a 1.5 MHz frequency; 1 kHz repetition rate; 200 μs pulse duration; and 30 mW/cm^2 spatial-average–temporal-average intensity (Azuma et al. 2001). The application of the LIPUS started 2 wk after the operation when the operative wound was cured. After both ends of the strut allograft were marked on the skin under an image intensifier, the ultrasound probe was applied with coupling gel on each end of the allograft from the surface of the femur. Treatment was given for 20 min/d at each site until complete bridging had been accomplished between the host femur and the allograft. The patients continued the LIPUS application after discharge from the hospital.

Standard radiographs of the anteroposterior and lateral views were taken after surgery at 2, 4, 6 and 8 wk, at 3, 6, 9 and 12 mo, and at 3 or 6 monthly intervals thereafter. Three surgeons (H.A., T.I. and H.O.) assessed the radiographs independently, and they noted the time of the appearance of the first bridging callus and of complete bridging. The presence of radiolucent lines at the cement-bone or cement-stem interface was recorded, as well as the presence of any femoral osteolysis, cortical hypertrophy, cement fractures or proximal femoral resorption (Engh et al. 1987). Loosening of the stem was defined according to the criteria of Harris and McGann (1986): Stem subsidence equal to or greater than 3 mm; cement fracture; a complete radiolucent line equal to or greater than 2 mm; or a radiolucent line in zone I equal to or greater than 2 mm. Hip function was evaluated using the Japan Orthopaedic Association hip scores.

This study was conducted with the approval of the Research and Ethics Committee of Kyoto University, Kyoto, Japan, and informed consent was obtained from all participants as per the WORLD Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Patients, 2008.

Statistical analysis

Statistical comparisons were performed using a t test (Aspin–Welch) with significance at $p < 0.05$.

RESULTS

The mean operative time and intra-operative blood loss were 239 min (range: 173–366 min) and 1226 g (range: 100–2092 g) in the LIPUS treatment group, and 327 min