

Long Gamma Nail Stabilization of Pathologic and Impending Pathologic Femur Fractures

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Abstract: Thirteen long Gamma nails were utilized without adjunctive bone cement in 11 patients for stabilization of 12 impending pathologic fractures and 1 pathologic fracture in the setting of metastatic disease (10 femora) and fibrous dysplasia (3 femora) of the proximal femur. Each femur was reamed to 18 mm proximally and 13 mm distally to accept the 17-mm diameter proximal portion and the 11-mm distal portion of the nail. Mean operative time was 104 minutes (range 60–237 minutes). Mean estimated blood loss was 304 cc (range 100–1,000 cc). All but one of the patients were allowed immediate full weight bearing on the operative limb. Overall International Society of Limb Salvage (ISOLS) ratings were excellent following seven procedures, good following five procedures, and poor following one procedure. Good to excellent pain relief was achieved following 11 of the 13 procedures. Either improved ambulatory capacity or good to excellent pain relief was achieved following 12 of the 13 procedures. Improvement by at least one ambulatory level was seen in 8 of 11 patients and following 10 of 13 procedures. One significant intraoperative complication, comminution of the already severely compromised intertrochanteric region, was encountered in one patient with metastatic lung carcinoma. The long Gamma nail has the advantages of percutaneous insertion through the tip of the greater trochanter, secure fixation in the proximal femur, and the ability to allow early weight-bearing ambulation. These advantages make it a desirable implant for stabilization of pathologic and impending pathologic femur fractures.

Introduction

The femur is the most common long bone site for metastatic tumors. Within the femur, the proximal portion is most commonly affected and is particularly prone to fracture or impending pathologic fracture. Benign lesions such as fibrous dysplasia may also involve the proximal femur and result in pain due to stress fractures or impending pathologic fracture. Appropriate operative stabilization of these proximal femoral lesions may prevent fracture, relieve pain, and preserve or restore function.

Stabilization of proximal femoral pathologic lesions, particularly those in the intertrochanteric and subtrochanteric area, presents unique challenges. Compressive forces in the proximal femur may exceed six times the body weight [8]. The need for adjunctive preoperative or postoperative ra-

diotherapy to prevent local disease progression may compromise the skin condition, resulting in wound healing problems.

The Zickel nail was the earliest device used with success for treatment of pathologic subtrochanteric femur fractures [26]. However, implantation of the Zickel nail is technically demanding and has been associated with cortical penetration, comminution of the greater trochanter, malrotation, shortening, and malposition [16,19,26]. The Zickel nail has largely been replaced by contemporary reconstruction nails. Reconstruction nails are modifications of interlocking fracture nails designed for proximal fixation within the femoral neck/head region and have instrumentation to allow accurate proximal locking screw placement [9,23]. The failure mode of the reconstruction nail with dual proximal interlocking screws in biomechanical testing is most frequently by cut out of the screws in the femoral head [6,14]. In addition, accurate placement of the dual screws within the femoral neck and head is technically demanding [4].

A number of third-generation reconstruction devices are now in use as alternatives to the standard reconstruction nail. These devices, which gain proximal purchase by way of a single larger screw or blade device within the femoral head/neck region, appear in biomechanical testing to have improved purchase within the remaining bone but have resulted in unique failure modes [1,5,7,11,15,20,21,25]. The spiral blade has been noted to fail both in the laboratory and in clinical use by blade breakage and migration [3,22,24]. Consequently, use of the spiral blade in osteoporotic patients who require early weight bearing has been questioned [3].

Our purpose is to report the experience at a single institution with another third-generation femoral reconstruction device, the long Gamma intramedullary nail, in patients with proximal femoral bone lesions in order to identify its advantages and the problems associated with its usage. This is the first series on use of this device for patients with pathologic lesions.

Methods

Medical records and imaging studies from the State University of New York Health Science Center at Syracuse and the Veterans Administration Hospital in Syracuse, New York, between January 1997 and August 1998 were re-

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viewed. Eleven patients who had 13 long Gamma nails placed in the treatment of pathologic fractures or impending pathologic fractures of the femur were identified. No patients were excluded. Operative indications, intraoperative findings, technical difficulties and complications, postoperative course, pain relief, function, and late complications were noted.

The long Gamma nail (Howmedica; Rutherford, NJ) is an unslotted intramedullary nail with a distal cloverleaf profile. The nail is 17 mm in proximal diameter, tapering to 11 mm distally. The proximal portion of the nail accommodates a 12-mm lag screw that can be placed at angles of 125, 130, or 135 degrees. All patients in this series had 130-degree implants placed. The lag screw incorporates a sliding lock to provide compression when desired. The nail incorporates 10 degrees of proximal anteversion relative to its 3.0-m radius of the curvature distal bow. The distal end of the nail has two parallel holes to accept locking bolts.

For patients with impending fracture, the procedure was performed with the patients positioned supine on a radiolucent table with a soft roll beneath the operative hip. For the single patient with a displaced subtrochanteric fracture, the procedure was performed supine on the fracture table with the operative lower extremity in traction through a foot plate and boot. An incision was made starting at the tip of the greater trochanter and extending 6 cm proximally. The incision was deepened through the subcutaneous tissue and fascia lata. The fascia overlying the abductor musculature was then split minimally to expose the tip of the trochanter. Minimal disruption of the muscle fibers was necessary. An awl was used to gain entry into the tip of the trochanter at the junction of the anterior third and posterior two thirds as confirmed by fluoroscopy. Straight T-handle hand-held starter reamers were utilized to enlarge the hole proximally and to extend it down through the medullary canal of the subtrochanteric region. A guide wire was passed into the medullary canal, across the fracture site or lesion(s), and into the distal intercondylar region. The distal femur was reamed to 13 mm and the intertrochanteric region to 18 mm to accommodate the wider proximal portion of the nail. Nail length was chosen based on measurement of the intramedullary portion of the guide rod intraoperatively. It was compared to contralateral femoral length based on scanograms of the contralateral femur when available. The appropriate length nail was inserted by hand under fluoroscopic guidance predominately without use of the mallet. The projected axis of the lag screw was observed during nail placement. After appropriate positioning of the threaded Kirschner wire through the proximal interlocking screw jig, the hole for the lag screw was reamed and the appropriate length lag screw turned into position by hand. Distal locking screws were placed using a radiolucent drill and fluoroscopic guidance when deemed necessary.

Demographics for the 11 patients, in whom thirteen 130-degree long Gamma nails were placed, are as follows. Seven of the patients were male and four were female. Mean patient age was 61 years (range 37–72 years). The underlying bone diseases included fibrous dysplasia (three nails

in three patients), prostate carcinoma (four nails in three patients), lung carcinoma (two nails in two patients), renal cell carcinoma (one nail), breast carcinoma (one nail), and unknown primary carcinoma (two nails in one patient).

Indications for the procedure included an intertrochanteric pathologic fracture in 1 patient and 12 impending pathologic fractures in 10 patients. Impending pathologic fractures in 11 femurs met the minimum criteria as defined by Mirels [18]. The remaining femur was stabilized prophylactically following open biopsy and curettage of a painful subtrochanteric bone lesion of the proximal femur found to be fibrous dysplasia. The bone disease involved the subtrochanteric (10 femurs), intertrochanteric (2 femurs), neck (5 femurs), and shaft (4 femurs) regions alone or in combination.

Preoperative ambulatory status was nonambulatory prior to four intramedullary roddings in three patients, including one patient with a displaced pathologic intertrochanteric fracture, one with a contralateral pathologic acetabular fracture, and another with functionally limiting bilateral proximal femoral disease. Prior to the remaining nine procedures, preoperative ambulatory status included a walker in two, crutches in three, a cane in one, and no aids in three. All patients rated their pain preoperatively as moderate to severe.

Prophylactic antibiotics were administered preoperatively and continued for 24–48 hours postoperatively. Preoperative embolization was accomplished for the patient with a renal cell carcinoma. Supplementary bone cement was not utilized in any patient. Anticoagulation therapy included aspirin or coumadin for 6 weeks. All patients were out of bed to a chair on the first postoperative day and began physical therapy for ambulation on the second postoperative day. All but one patient were allowed immediate full weight bearing postoperatively. That patient had a subtrochanteric femur fracture and experienced comminution of the intertrochanteric region intraoperatively. Postoperative external beam radiotherapy to the entire femur was accomplished in those patients not previously irradiated in that region.

The scoring system of the International Society of Limb Salvage (ISOLS) for the proximal thigh, hip, and pelvis region was utilized to rate overall function. The overall score is a compilation of seven categories, including motion, pain, stability, deformity, strength, functional activity, and emotional acceptance. For the purposes of this study, a percentage of each patient's score was calculated relative to the most possible points for the categories in which data had been collected on that patient. An overall excellent result was considered greater than 85% of normal, a good result greater than 75% of normal, a fair result greater than 55% of normal, and a poor result 55% or less of normal.

Results

Overall mean duration of follow-up was 4.9 months (range 2–11 months). At latest follow-up, six patients had succumbed to their underlying carcinoma at 2–11 months postoperatively (mean 4.4 months). The remaining five pa-

tients were alive with disease at a mean follow-up of 5.6 months (range 3–9 months).

The average operative time for the procedure was 104 minutes (range 60–237 minutes) including time for biopsy and frozen section review when performed. One of the two bilateral nailings was done under a single anesthetic. The second bilateral procedure was done staged because the lesions required treatment at different times.

The average estimated blood loss during the procedures was 304 cc (range 100–1,000 cc). The lowest postoperative measured hemoglobin for 7 of the 13 procedures for which this information was available ranged from 6.9 to 11.7 mg/dl with a mean of 9.1 mg/dl (normal 13.5–18.0 mg/dl). Mean decrease in hemoglobin level preoperatively to postoperatively following seven procedures for which this information was documented was 3.7 mg/dl (range 0.3–5.1 mg/dl). The mean lowest postoperative hematocrit value following nine of the procedures for which this information was available was 26.9% with a range of 20.7–35.6% (normal 36–45%). Mean decrease in hematocrit value preoperatively to postoperatively following nine procedures for which this information was documented was 10.6% (range

0.7–25.4%). Transfusions of packed red blood cells (median of 2 U) were necessary following 8 of the 13 procedures, including following the treatment of a displaced subtrochanteric fracture, a metastatic renal cell carcinoma, and each of three procedures in two patients who underwent bilateral roddings.

Overall maximum ISOLS rating achieved postoperatively was excellent following seven procedures, good following five procedures, and poor following one procedure. Excellent scores ranged from 89.0 to 100% normal. Good scores ranged from 80.0 to 85.0% normal. Mean rating as a percentage of total possible score for all 13 patients was 86%, with a range of 37–100%.

Pain relief was good (four) to excellent (seven) following 11 of the 13 procedures. One of the patients with fibrous dysplasia obtained only fair relief and continued to be bothered by greater trochanteric bursitis at latest follow-up. Pain relief in the patient with the intertrochanteric fracture was rated poor, but his pain was improved sufficiently to allow active participation in physical therapy on the normal schedule.

The maximum ambulatory level achieved postoperatively



Fig. 1. Single major complication. **A:** Anteroposterior radiograph of proximal femur showing displaced pathologic subtrochanteric fracture in patient with metastatic non-small cell lung carcinoma. **B:** Postoperative radiograph following stabilization with long Gamma nail. Intraoperative difficulty with intertrochanteric fragmentation was encountered during placement. An open cerclage wiring was performed. The patient had poor pain relief postoperatively, but he was able to ambulate with a walker prior to his death at 6 weeks postoperatively due to progressive metastatic disease. Adjunctive bone cement and proximal femoral replacement megaprosthesis reconstruction are other viable alternatives when this degree of proximal femoral bone destruction is encountered.

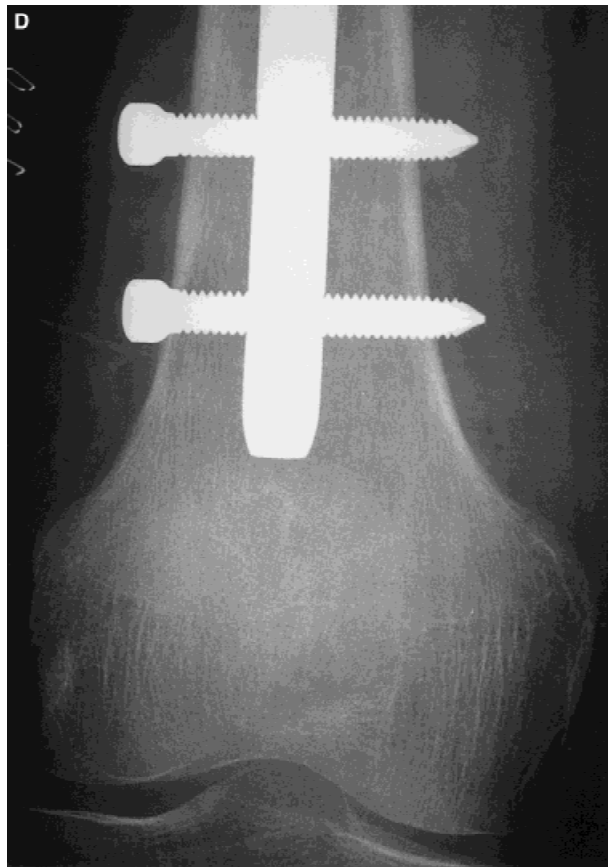




Fig. 2. Anterior cortical penetration. Anteroposterior radiographs of (A) hip and (B) proximal femur showing impending pathologic femur fracture in patient with metastatic prostate carcinoma. C: Postoperative anteroposterior radiograph of the hip following placement of the long Gamma nail. D: Postoperative anteroposterior radiograph of the distal end of the femur showing apparent acceptable position of two distal interlocking screws. However, review of the lateral radiograph (E) shows that the distal tip of the nail has partially penetrated the anterior cortex. Despite this finding, the patient was allowed immediate full weight bearing postoperatively and progressed to excellent pain relief without loss of fixation or fracture.

was independent without aids following seven procedures, assisted ambulation with a walker following four procedures, and assisted ambulation with a cane following two. Eight of the eleven patients, including all those who were nonambulatory or walked only with ambulatory aids preoperatively, improved at least one ambulatory level following 10 of the 13 procedures. Only one patient, who died 2 months postoperatively, failed to regain his preoperative ambulatory independence. Two additional patients who walked independently preoperatively returned to that level. One patient who had improved from a preoperative bedridden status to postoperative independent ambulation with a walker subsequently required a wheelchair secondary to impending paraplegia from disseminated inoperable spinal metastases just prior to her death. A second patient who had improved from walker ambulation to independent ambulation with a cane postoperatively later suffered lower extremity paralysis from a pathologic spinal fracture that left him

bedridden awaiting operative intervention at latest follow-up.

Intraoperative complications occurred during 3 of the 13 procedures. Two of these were considered minor complications, one a major complication. The major complication occurred in the patient with extensive destruction of the proximal femur by metastatic non-small cell lung carcinoma and a pathologic subtrochanteric fracture. He incurred fragmentation of his severely weakened proximal bone (Fig. 1). This necessitated open cerclage wiring supplemental fixation. Cementation was not utilized as an adjunct to fixation in this patient. This patient was the only patient whose postoperative pain relief was poor. A second patient experienced slight nail penetration of the anterior cortex of the distal metaphyseal femur just proximal to the trochlear groove during nail placement. This patient achieved excellent pain relief, remained asymptomatic during follow-up, was able to progress quickly to immediate full weight-bearing status with a cane, and required no additional fixation (Fig. 2). The third complication was displacement of an impending intertrochanteric fracture that occurred during positioning for the procedure. This latter patient achieved good pain relief and his postoperative course was not altered. There were no postoperative complications.

No failure of the hardware due to breakage, loosening, migration of the lag screw, or breakage was noted at the latest follow-up. There were no distal fractures. Position of the distal tip of the nail was most frequently in the anterior third (Table 1).

Discussion

The peritrochanteric region of the femur is an area of high stress and frequent involvement by metastatic disease and fibrous dysplasia, often resulting in pathologic or impending pathologic fracture, pain, and disability. Stabilization of bone lesions in these areas prior to fracture results in an improved quality of life. The expected duration of survival for patients with metastatic disease also continues to improve, making the need for stable and durable fixation crucial.

The devices typically employed for stabilization of peritrochanteric pathologic and impending pathologic fractures have evolved over time. The first successful implant widely utilized in this situation was the Zickel nail, a rigid intramedullary device with a proximal hip bolt placed through the nail into the femoral neck region [26]. The Zickel nail

Table 1. Position of long Gamma nail tip within distal femur on lateral view

Position	Number (%)
Anterior one third	10 (77)*
Central one third	3 (13)
Posterior one third	0 (0)
Total	13 (100)

*Cortical penetration occurred in one case.

was very successful, particularly when utilized with cement. However, it was associated with shortening and loss of rotational control without bone cement due in part to the lack of distal interlocking capability [19,26]. In addition, cortical penetration, comminution of the proximal femur, malrotation, and malposition of the proximal locking device have been reported [16].

The second generation of reconstruction nail includes the prototype Russell-Taylor reconstruction nail (Smith and Nephew Richards; Memphis, TN) as well as spin-offs, including the ZMS (Zimmer; Warsaw, IN), the Uniflex (Biomet; Warsaw, IN), and the Alta CFX (Howmedica). The common denominators of these nails are the dual interlocking screw proximal fixation in the femoral neck and the capability of distal interlocking. These nails were initially introduced to extend the indications for interlocking femoral intramedullary nail fixation to include concomitant femoral neck and shaft fractures. Their use for pathologic and impending pathologic peritrochanteric fractures has become commonplace. These nails are typically placed in an antegrade reamed fashion, with over-reaming distally by 2 mm to allow ease of positioning of the proximal screws within the femoral neck. These devices have resulted in less complications and improved ease of insertion compared to the Zickel nail to the extent that they have been the standard treatment for subtrochanteric pathologic fractures since their introduction.

Weikert and Schwartz [23] reported favorable results using the Russell-Taylor reconstruction nail for treatment of impending pathologic subtrochanteric fractures in 10 patients. All patients reported symptomatic relief prior to hospital discharge but were asked to protect their weight bearing over the ensuing 6 weeks. Subsequent to progressing to full weight bearing, one half of their patients advanced to an improved level of ambulation. Only one complication, a deep venous thrombosis, occurred. There were no failures of the nail. Karachalios et al. [13] reported similarly good results with the Russell-Taylor and similar reconstruction nails for 14 patients with pathologic subtrochanteric fractures. Eleven of their patients were allowed initial full weight bearing with crutches. Two patients were mobilized with walkers and one was kept non-weight bearing for 6 weeks. All patients achieved marked reduction in their pain and recovered painless motion of the hip and knee. None of the nails in this series failed, but one patient suffered a fatal air embolism during reaming. Miller and Biermann [17] recently reported another series of 23 reconstruction nails utilized for pathologic involvement in the femoral shaft. Nineteen patients achieved good or excellent pain relief and 14 patients were able to ambulate without ambulatory aids. Four complications did not require reoperation.

In contrast to these studies on the use of reconstruction nails in the pathologic setting, frequent complications have been reported with their use for nonpathologic fractures [12]. Kang et al. reported a 35% complication rate in 37 patients with proximal femoral fractures. Complications occurred in three of four ipsilateral femoral neck and shaft fractures and in 6 of 18 intertrochanteric fractures with di-

aphyseal extension. Complications included nonunions, leg length discrepancies of greater than 2.5 cm, varus deformity greater than 10 degrees, nail breakage, and proximal screw back-out. Two technical difficulties accompanying these complications were lack of anatomic reduction in intertrochanteric fractures with diaphyseal extension and short proximal interlocking screws. In the laboratory, these types of nails may fail by screw cut out in the femoral head, suggesting that proximal fixation may be compromised, particularly when proximal bonestock is less than ideal [6,14].

More recently, so-called third-generation variations of the reconstruction nail have become available and are being utilized for pathologic and impending pathologic femur fractures [1,5,7,11,15,20,21,25]. The common denominators for these devices are the capability for distal interlocking and the use of a single device proximally for secure fixation in the femoral neck and head. These devices differ based primarily on the proximal interlocking device.

The unreamed spiral blade interlocking nail (Synthes) utilizes a single low-profile spiral blade device to secure proximal fixation and conserve bone loss in the femoral neck. These solid core flexible titanium nails were designed to be placed antegrade without reaming, thus theoretically diminishing blood loss and embolic phenomena. Both in biomechanical laboratory testing and in clinical usage, these devices have been reported to fail by cut out of the spiral blade, by migration, and by bending or breakage of the blade device, making their use in pathologic subtrochanteric fractures suspect [3,6,22,24]. Direct biomechanical comparison with three different reconstruction nails in two independent studies favored the reconstruction nails over the spiral blades in each case [6,24].

In a series of 28 fractures treated using the unreamed spiral blade interlocking nail, 16 of which were associated with metastatic disease, Broos et al. [3] reported five mechanical complications in four patients. One patient with a metastatic fracture experienced breakage of two spiral blades. Migration was encountered three times, twice requiring reoperation. By contrast, Hecht et al. [11] reported good results on 27 spiral blades implanted in 24 patients for pathologic lesions. None of their devices failed, although one spiral blade did cut out of the anterior bone during placement (Table 2).

Long intramedullary hip screw devices are the second category of third-generation reconstruction nails. They utilize a single large bore hip screw proximally, similar to the dynamic hip screw, and have distal interlocking capability. In biomechanical laboratory testing, the Richards long intramedullary hip screw (Smith and Nephew Richards) was found to be inferior to the Russell-Taylor reconstruction nail due to failure by bending of the proximal portion of the thin 10-mm long hip screw nail at significantly lower peak loads than that of screw cut out by the Russell-Taylor nail [14]. Favorito and McGrath [7] reported on the use of the Richards long intramedullary hip screw in 13 patients with pathologic or impending pathologic fractures. Three of

Table 2. Comparative parameters between three third-generation reconstruction type femoral interlocking nails*

Nail device manufacturer	Parameter					
	No.	Fx	Imp	Reamed	Operative time (minutes)	EBL (cc)
URSB (Synthes)	27	5	22	0 [†]	129 (80–180)	324 (75–1,000)
LIHS (Smith and Nephew Richards)	13	7	6	2 [‡]	110	280 [§]
LGN (Howmedica)	13	1	12	13	104 (60–237)	304 (100–1,000)

*No., number nails; Fx, number of pathologic fractures; Imp, number of impending pathologic fractures; Reamed, number of nails placed by reaming distally; EBL, estimated blood loss; URSB, unreamed spiral blade interlocking nail; LIHS, long intramedullary hip screw; LGN, long Gamma nail.

[†]Specific number of nails placed without reaming not stated in abstract, but nail designed for unreamed usage.

[‡]All of these nails were reamed proximally, but only two required distal reaming for the 10-mm diameter distal nail portion.

[§]Range not available.

seven fractures healed at 12-week follow-up and none of the devices failed (Table 2).

The long Gamma nail utilized in this study is the latest of these third-generation reconstruction intramedullary nail devices. It was first introduced in 1988 as a custom implant in response to the problem of shaft fractures experienced at the distal end of the standard length Gamma nail [25]. Stapert et al. [21] reported 92 patients treated with the initial custom long Gamma nail for complex and combined fractures of the proximal femur. Despite complications in 25 cases, 88 patients were able to walk independently at final analysis. The custom nail had a relatively rigid distal portion, a 17-mm proximal diameter, a 12-mm distal diameter, and a 135-degree angle hip screw. Particularly concerning problems encountered were “fissure” of the shaft by introduction of the nail in seven cases, fracture of the shaft by introduction of the nail in five cases, and cut out of the nail in one case. The fissure and fracture complications were attributed to rigidity of the distal portion of the nail, an implant problem that has been addressed in the current implant design. The underscored advantages of the implant were its closed insertion through the tip of the greater trochanter and the ability to allow immediate full weight bearing in all cases [21].

More recent reports detail the results following use of the currently available off-the-shelf long Gamma nail. Almodovar et al. [1] achieved 90% good results in their analysis of 30 patients treated with these newer long Gamma nails. Problems with fractures were much less frequent in this series, with only one diaphyseal fracture and one calcar fracture. One hip screw was placed outside of the head. Di Puccio et al. [5] reported one nail breakage and 17 unions within 6 months among 18 long Gamma nails in a series of combined femoral neck and shaft fractures, unstable comminuted intertrochanteric-subtrochanteric fractures, and pathologic subtrochanteric fractures. All patients had been allowed early weight bearing. In a multicenter European study reporting use of the long Gamma nail in 120 patients, 25 of whom had metastatic lesions, 60% of patients had returned to normal activities by 6 months postoperatively [15]. There were no fractures reported in this series, but three screw migrations and one broken screw occurred.

To our knowledge, there are no previously published studies exclusively examining the long Gamma nail for use in pathologic or impending pathologic fractures. Results reported here demonstrated good or excellent pain relief following 85% of the procedures. There was also an improvement over preoperative ambulatory status in 73% of our patients, with only one major intraoperative complication. The consistently anterior position of the distal tip of the nail, which in one case partially penetrated the cortex, is concerning. However, we did not encounter any shaft fractures, screw migration, screw cut out, or breakage in this series. The advantages of the long Gamma nail are the percutaneous insertion site into the tip of the greater trochanter and the secure fixation of the hip screw proximally that allowed immediate full weight bearing in all but one of our patients. The concern regarding increased blood loss with reaming for placement of these nails was not borne out in our estimated blood loss, which was comparable to two series in which other third-generation nails were placed with minimal or no reaming (Table 2). The percutaneous insertion of the nail through the trochanteric tip with minimal disruption of the abductors likely decreases blood loss for this portion of the procedure when compared to nails inserted through the piriformis fossa.

The long Gamma nail offers an attractive alternative for treatment of impending or pathologic fracture. The ability to allow early weight bearing following placement of a long Gamma nail is an advantage to patients with pathologic fractures, particularly those with metastatic disease who have a shortened lifespan. Early problems with distal femoral diaphyseal fractures associated with the custom long Gamma nail appear to have been largely eliminated by design modifications. Additional modification of the nail design to decrease the radius of curvature to 2.5 m would likely decrease the consistently anterior position of the distal tip and completely eliminate anterior penetration. Biomechanical laboratory testing in comparison to the second-generation reconstruction nails is needed. The need for adjunctive cement with this device is, as with each of the modern reconstruction nail devices, not well established. Its previously documented efficacy as an adjunct to fixation of pathologic fractures should be considered when bone-to-

bone contact cannot be reestablished by closed reduction and nailing alone [2,10].

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