

Congenital Pseudarthrosis of the Tibia

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► ABSTRACT

The results of treatment of congenital pseudarthrosis of the tibia (CPT) are frequently complicated by failure to achieve union, refracture, deformity, leg length discrepancy (LLD), ankle stiffness and foot deformity. Although the cause of CPT remains unknown, recent reports confirmed that the periosteum is the primary site for the pathologic processes in CPT. Recent evidence demonstrated underproduction of bone morphogenetic protein (BMP) by osteoblasts and overactivity of osteoclasts. On the basis of the new pathologic evidence Paley created a combined pharmacologic and surgical treatment in which a cross union between the tibia and fibula is created. This method has the highest union rate with the lowest refracture rate and shall be referred to as the Paley X-UNION protocol. This protocol includes all of the following in the prescribed order: preoperative bisphosphonate intravenous infusion (Zoledronic Acid), surgical excision of the diseased periosteal fibrous hamartoma, intramedullary (IM) nailing of both the tibia and fibula combined with or without subcutaneous locking plate fixation, subtotal iliac crest bone harvesting to harvest a large volume of cancellous bone, subiliacus muscle periosteal graft harvest, placement of a meshed periosteal graft around the CPT, autogenous cancellous bone grafting between the tibia and the fibula and around the CPT to create a tibio-fibular cross union, BMP2 placement around the graft, and circular external fixation if a locking plate is not used. Secondary procedures for angular correction with hemiepiphysiodesis at the proximal or distal tibial physis and rod exchange to protect the healed tibia are frequently necessary. Lengthening to treat LLD is done in older children either at the time of treatment or as a separate procedure.

► INTRODUCTION

Congenital pseudarthrosis of the tibia (CPT) remains one of the most challenging and dreaded conditions confronting pediatric orthopedic surgery. Over half the cases are associated with neurofibromatosis, ten percent with fibrous dysplasia or Campanacci's osteofibrous dysplasia and the remainder referred to as idiopathic. CPT has a tendency to refracture until skeletal maturity. Fractures can even occur in adults. The refracture incidence is highest at younger ages. Neurofibromatosis is considered a negative prognostic factor. Younger age of treatment is also a negative prognostic factor. This may be related to the activity of the pathologic tissue being greater at a younger age when growth rate and metabolism are at their greatest. It may also be a function of the diameter of the bone, which is smaller at a younger age and therefore more prone to stress related fracture. Failed previous treatment is another negative prognostic factor.

There are many techniques for the management of CPT dating back over 100 years.¹ McFarland² used a bypass fibular graft, Boyd³ and Boyd and Sage⁴ recommended a double onlay graft taken from the opposite tibia combined with autologous iliac crest graft, Charnley⁵ employed intramedullary (IM) rods, and Sofield⁶ added fragmentation and reversal of fragments. Campanacci and Zanolli⁷ described a "fibula pro tibia" technique with fibular fixation to the pseudarthrosis site. Other methods include direct current or pulsed electromagnetic field, ipsilateral transfer of the fibula or contralateral free vascularized fibular transfer, circular external fixation, IM rodding, and combined external fixation and IM rodding. More recently, bone morphogenic protein (BMP)⁸ and bisphosphonate therapy^{9,10} have been used. The results of all these methods have been variable. Refracture rates are high with all of these methods.

► PATHOLOGY OF CPT

The pathology of CPT is still poorly understood. During the past 100 years, many theories have been suggested to explain the development of the pseudarthrosis. Today, interest concentrates mainly on the pathologic changes in the periosteum.¹¹ Codivilla¹ recognized that the periosteum is diseased more than 100 years ago.

McElvenny¹² reported a thickened, adherent periosteum that constricted the tibia and fibula causing atrophy, leading to fracture and pseudarthrosis. Boyd³ and Boyd and Sage,⁴ based on amputated specimens, suggested that CPT was caused by osteolytic fibromatosis. Blauth et al¹³ in a study of 10 patients with CPT, postulated that the thickened periosteum was caused by myofibroblast overgrowth.¹⁴ A more recent report¹¹ identified neural-like cells that surround the small periosteal vessels causing narrowing and obliteration of these vessels. They postulated that this leads to hypoxia of the subperiosteal bone with subsequent resorption, fracture and nonunion.

Cho et al¹⁵ showed that periosteal cells in the hamartoma of CPT have decreased osteoblastic responses to BMP-2. In contrast the osteoclastic activity of the periosteum was significantly higher than that of controls. They concluded that failure of healing as

well as resorption of bone graft is related to increased osteoclastic activity and decreased osteoblastic activity of the CPT periosteum compared to normal periosteum.

Schindeler et al showed that NF1(+/-) (NF positive) mouse cells had less osteogenic potential than NF1(+/+) (NF negative) cells (controls). There was much less bone formation in response to BMP in the NF positive cells compared to the NF negative cells. Co-treatment with zolidronic acid (ZA) lead to synergistic increase in bone formation in both groups. They concluded that biphosphonate-BMP combination therapy was superior to BMP therapy alone.

► PERIOSTEUM

Resection of hamartomatous fibrous tissue is part of many treatment protocols, but it does not ensure healing or prevent refracture. Codivilla recommended osteo-periosteal grafting more than 100 years ago.¹ Cambras (circa 1977, personal communication 1996) treated CPT with bone and periosteal grafting from the child's mother, emphasizing the role of the periosteum to cure the disease. Paley¹⁶ proposed periosteal grafting as a treatment option in 1995 based on observations he made during his first 8 years of treating this condition.¹⁷ Paley's periosteal grafting method was first published in a doctoral thesis by El Rossasy¹⁸ in Egypt in 2001 and then in a book edited by Rozbruch in 2007.¹⁹ Paley's periosteal grafting method was used and reported on by Michael Weber¹⁹ from Germany and Franz Grill from Austria [IPOS meeting 2006, Orlando, Florida]. A two-center study combining the experience with periosteal grafting from Paley and Kocaoglu was published in 2008 by Thabet et al.²⁰

The Paley method of periosteal grafting described by Thabet et al²⁰ was the culmination of twenty years of experience in the treatment of CPT. Paley's first published report on CPT was in 1992.²¹ Follow-up of those and additional early Paley treated patients reported in El Rossasy's doctorate thesis demonstrated a high refracture and retreatment rate. The initial treatment was using the Ilizarov method with bone grafting of the CPT site combined with hamartoma resection. The healing rate was nearly 100% but the refracture rate was over 50%. When an IM rod was added to the Ilizarov-bone grafting treatment the refracture rate dropped. Clearly the Ilizarov fixation method was excellent at obtaining union but failed to maintain union. The IM rod was excellent at maintaining union and decreasing refracture. This was also the conclusion of the multicenter EPOS study by Grill et al.²² The efficacy of the IM rod was also increased by rodding both bones in the leg rather than just one.

Based both on the literature and the author's personal experience the other two factors that significantly helped decrease refracture were increasing the cross sectional area of union and eliminating angulation especially at the CPT site. Combining all of these principles, Paley proposed the treatment method that was studied in the two center study reported by Thabet et al.²⁰ Twelve of the twenty patients reported, were treated by Paley, while the other eight were treated by Dr. Mehmet Kocaoglu in Turkey using Paley's method. While the union was achieved in 100% there was a 40% refracture rate (8/20).

► THE PALEY X-UNION PROTOCOL (FIG. 1)

Successful treatment of most atrophic nonunions involves optimizing the mechanical and biologic environment of the pseudarthrosis site. Mechanical modalities include: correction of angular deformity, stability of fixation using external and/or internal fixation, increased bone width at the CPT site, and reinforcing the bone strength with intramedullary fixation of the tibia and fibula. Biologic modalities include resection of the fibrous hamartoma, resection of any hypovascular bone, improving the blood supply to the CPT site, and autogenous bone and periosteal grafting of the CPT site. The use of these mechanical and biologic modalities, lead to reliable union in 100% of cases. It did not, however, prevent refracture. Even the introduction of intramedullary nailing to reinforce the weak bone, reduced, but did not eliminate refracture.

What more could be done on both the biologic and mechanical aspects of CPT? Mechanically, I had already achieved union, reinforced the inside of the bone with an intramedullary rod in the tibia and fibula, and achieved as wide a union of each individual bone (tibia and fibula) as possible. Obviously, I could not straighten or reinforce the inside of each bone any better. I could however widen the union area by creating a bridge between the tibia and the fibula. In reviewing the radiographs of some of the cases that I had treated, that never developed a refracture, I noticed that some had a cross union between the tibia

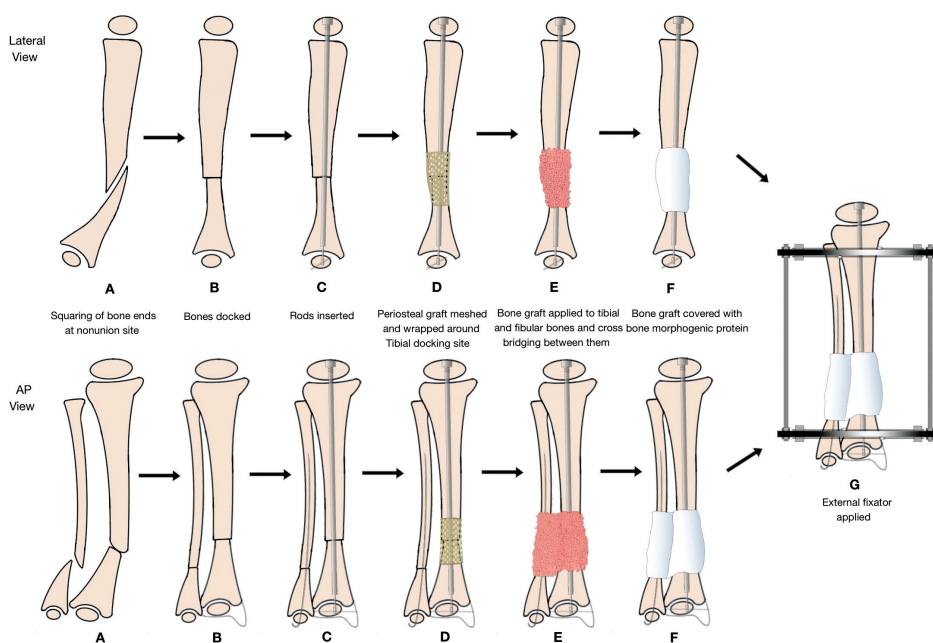


Figure 1

Paley X-UNION technique illustration.

and the fibula at the level of the CPT. I postulated that the large cross sectional area of union made it almost impossible to break the tibia. This may also account for why younger children refracture more easily, while older children have a lower incidence of refracture. The tibial cross section is very small at a young age but increases by orders of magnitude as the bone gets wider with increasing age. To achieve a cross union, it requires a large amount of autograft to be placed in between the tibia and fibula. This amount of autograft is not available from the anterior or posterior iliac crest of most young children. The only part of the pelvis that contains ample autogenous cancellous bone is the supra-acetabular region. To get to that region surgically, one would need to split the iliac crest past the narrow bottleneck of the iliac wing (Fig. 2). I developed the method to do this in 2002. At that time I was only bone grafting circumferentially around the tibia. Unintentionally, this generated a cross union in several of these patients. By splitting the two tables of the ilium, I could harvest bone from both the anterior and posterior aspects of the ilium, hollowing out the entire ilium down to the subchondral bone of the hip and triradiate cartilage, around the Gothic arch of the sciatic notch, to the cancellous bone of the posterior iliac crest as far

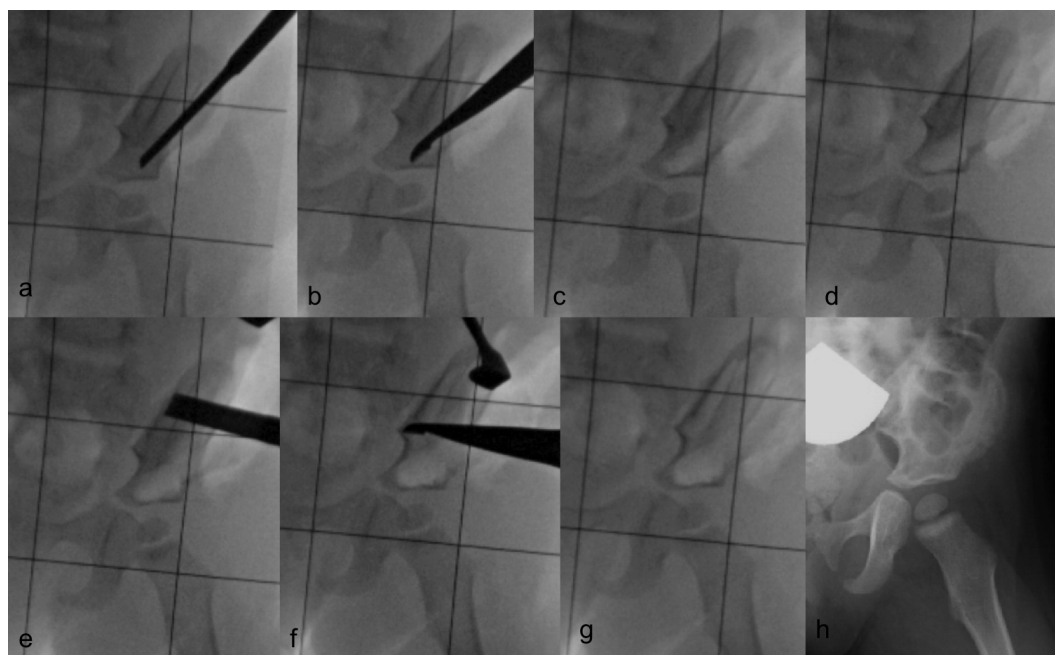


Figure 2

Bone graft harvest method: a) Iliac crest tables are split with a thin sharp osteotome from the anterior superior to the anterior inferior spine and then down to the level of the dome; b) a curette is used to harvest the cancellous bone from above the dome of the acetabulum; c,d) the anterior cancellous bone is harvested down to the dome and the triradiate cartilage; e) the crest is split down to the sacro-iliac region; f) the posterior iliac cancellous bone is curetted; g) the entire iliac crest has been decancellousized; h) radiograph six months later showing complete reconstitution of the iliac cancellous bone.

as the subchondral bone of the sacro-iliac joint. I call this decancellousization of the ilium (Fig. 2). Even in a 12-month-old infant decancellousization yields up to 15 cc, while in an older child as much as 45 cc can be harvested. With this large amount of cancellous bone graft, creating an intentional cross union between the tibia and fibula is consistently possible as long as the bone graft is not resorbed. To prevent resorption, I started to pretreat the children with Zolidronic Acid (ZA) two weeks prior to surgery. This allowed the Zolidronic Acid to be absorbed by the cancellous bone of the ilium. This made the cancellous bone of the ilium non resorbable. I also wanted to boost the osteogenic response of this cancellous bone. We started using BMP2 for this purpose. Looking at this combined treatment with ZA and BMP2, it is obvious that we had downregulated the excessive osteolysis with ZA and upregulated the sluggish CPT bone osteogenesis with BMP. I began to use BMP2 and later ZA around 2004 to treat some of the refractures we were still seeing despite periosteal grafting and rodding. The rationale for this is well explained by the later publications of Cho et al 2008 and Schindler et al 2008.^{15,23} They showed that the soft tissue hamartoma around the CPT had excessive numbers of osteoclasts leading to an abnormal degree of osteolysis. They also showed that the response to BMP was more limited in NF. These publications supported the combined use of BMP2 with ZA in a synergistic fashion. This was the pharmacologic approach, I had intuitively started using since 2004.

In 2007, I first intentionally combined all of these techniques to create an intentional cross union between the tibia and the fibula. I pretreated with ZA, resected the hamartoma, rodded the tibia and fibula, decancellousized the ilium and harvested a periosteal graft. I then applied my 3 layer graft: periosteum cambium layer down around the already osteosynthesised CPT site; cancellous bone between and around the tibia and fibula; BMP2 over top the bone graft covered by soft tissues.

► PALEY X-UNION SURGICAL PROTOCOL (FIGS. 1,3)

Step 1: Preoperative biphosphonate infusion: Two weeks prior to the surgery the patient is given a Zolidronic Acid infusion intravenously (0.02mg/kg) over 30 minutes. One hour later calcium gluconate 60 mg/kg is given intravenously over the course of one hour. The patient is given 2 gm elemental calcium for 7 days and Vitamin D supplementation of 400 IU for 14 days.

Step 2: Prep and Incision (Fig. 3b): The patient is placed supine, with a bump under the ipsilateral buttock, on a radiolucent table. The entire lower extremity and hemipelvis are prepped and draped free. The leg is exsanguinated and tourniquet applied. The pseudarthrosis site is approached through an anterior longitudinal incision.

Step 3: CPT Periosteum Excision (Fig. 3b,c): The thick periosteum is incised longitudinally. The periosteal incision ends at the point at which the periosteum thins to a normal thickness. Dissection between the periosteum and the surrounding soft tissues is carried out circumferentially around the tibia. On the lateral side avoid injury to the anterior tibial artery and deep peroneal nerve that can be enveloped in this fibrous hamartoma.



Figure 3 a

AP and Lateral radiographs of six year old boy with CPT



Figure 3 b

Anterior longitudinal incision for exposure and circumferential hamartoma resection

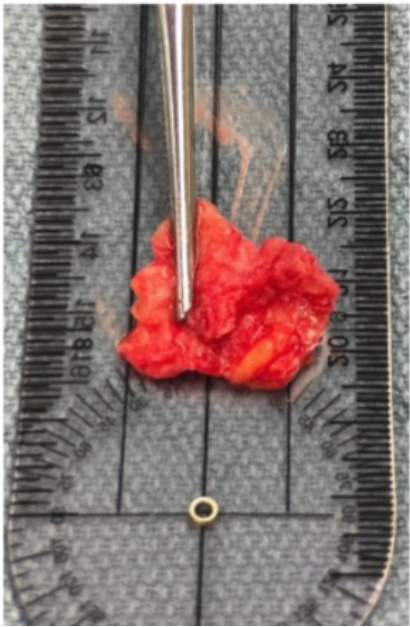


Figure 3 c

Hamartomatous tissue after resection



Figure 3 d

Exposure of fibula

On the postero-medial side beware that the periosteum may appear contiguous with the deep posterior compartment fascia. It is important to follow the periosteum around to the posterior side of the tibia and heading posteromedial into the deep posterior compartment and into the vicinity of the posterior tibial neurovascular bundle. It is safer to remove the hamartoma in pieces rather than try and remove it as one circumferential piece.

Step 4: Dissect down along the interosseous membrane to the fibula. Resect a large window of this interosseous membrane taking care not to injure the peroneal vessels. This exposes the deep posterior compartment fat plane, to the space between the bones. If the fibula is intact cut the periosteum at the level of the CPT. If the fibula is broken then remove the fibrous hamartoma from around the fibula.

Step 5: CPT bone end preparation: The pseudarthrosis of the tibia is separated apart by removing any fibrous tissue between the bone ends. Once disengaged the proximal and distal tibia will overlap relative to each other by straightening the bone ends. The amount of shortening resulting from this depends on the degree of previous fixed angulation and the amount of pre-existing contracture of the soft tissues.

Step 6: Fibular CPT/osteotomy preparation (Fig. 3d): The fibula may tether the tibia. If it is broken, separate the bone ends of the fibula and overlap them to allow the leg to realign. If the fibula is intact and there is significant overlap of the tibia and no angular deformity of the fibula, leave it intact. If the fibula is tethering the shortening needed in the tibia or if it has an angular deformity in the fibula, osteotomize the fibula at the same level as the CPT or at the apex of an angular deformity of the fibula. Allow the fibular bone ends to overlap as needed.

Step 7: Square off the bone ends of the tibia and fibula. Start with the tibia. Make sure the two bone ends are as wide as possible. Try and make the cuts so that the most sclerotic and atrophic parts of the tibia are resected. Try and minimize the resection. The intention is not to resect the CPT. The cuts are simply to bring two ends of the tibia together in a straight alignment position with the minimum amount removed. The intention is to also make the tibial cuts at a level that is as wide as possible to maximize the bone contact area. Alternatively, one bone end can be split and the other end invaginated inside of it. The wider end is split while the more atrophic end is invaginated. No resection is required if one end is split since the bones shorten as they invaginate. The split is created in such a way that it does not fracture either arm of the split. The tibia resembles the old-fashioned one-piece wooden clothes pin. The split is made by using a thin saw blade.

Step 8: Tibial Reaming (Fig. 3f): The tibia is drilled for insertion of a Fassier-Duval telescopic nail. A wire is drilled retrograde up towards the knee joint. It is brought out the knee joint so that it is centered on the AP and anterior on the lateral. A cannulated drill bit corresponding to the diameter of the nail to be used is drilled to create a channel for the nail. A wire is then inserted antegrade from the knee across into the distal bone segment. The cannulated drill is then drilled antegrade to and through the distal tibial physis but not perforating into the ankle joint. The length of this wire is then measured from the knee to



Figure 3 e
Predrilling of
intact fibula
with 1.5mm
wire



Figure 3 f
Antegrade
drilling for
Fassier-Duval
nail insertion



Figure 3 g
Male portion of FD nail customized for length
inserted down into the distal tibial epiphysis



Figure 3 h
Wire locking of male portion in distal
tibial epiphysis from medial side

the distal tibial epiphysis using two wires of the same length.

Step 9: Telescopic Nail Customization (Fig. 3g): Use a metal cutting saw to cut the male and female Fassier-Duval nails to the correct length.

Step 10: Fibular Drilling (Fig. 3e): Use a 1, 1.5 or 1.8 mm wire to drill retrograde up the fibula from the pseudarthrosis or osteotomy sites when present or from the lateral malleolus if the fibula remains intact. Then drill a hole antegrade from the pseudarthrosis or osteotomy site exiting the lateral malleolus. Bring the antegrade wire out the skin and leave it ready to be advanced retrograde into the predrilled hole in the proximal fibula.

Step 11: Tibial Telescopic Nail Insertion (Fig. 3g): Male part: Insert the precut male portion of the Fassier-Duval (FD) with the locking hole end into the epiphysis. It is preferable to use what is known as the Paley modification or LON version of the male FD nail. The screw ended male FD nail used for osteogenesis imperfect does not fix well into the small distal tibial epiphysis. Use the lockable male end described above instead. Lock this end with a 1.5 mm wire from the medial side of the epiphysis by magnifying the hole on the image intensifier (Fig. 3h). Once this wire is through the hole in the nail bring it out the lateral skin of the ankle. Curl the wire onto itself and then pull it back into the epiphysis (Fig. 3i). Then cut the wire flush with the skin on the medial side. Use a small tamp to advance this wire so it is flush with the medial cortex and does not protrude medially. Now remove the male inserter device.

Step 12: Tibial Telescopic Nail Insertion (Fig. 3j): Female part: Insert the precut female FD nail, capturing the male end in its cannulation. Screw the female end into the upper tibial epiphysis. Take care to use the fully threaded female end without the smooth extension.

Step 13: Locking plate application (optional): If using an external fixator (step 25), go to step 12. If using a locking plate, apply it now. The locking plate should be a low profile long straight plate that extends from the distal to the proximal tibia. Lock it with two to three screws on either side of the tibia with compression of the pseudarthrosis. Author's preferred plate is the Smith and Nephew EVOS plates (Fig. 3w,x).

Step 14: Retrograde fibular nailing: Resect the overlapping fibular ends as needed to bring the two ends into contact with each other at the length established by the tibial bone ends that are now fixed with the FD nail. Advance the lateral malleolar wire retrograde into the proximal fibula as proximal as possible (up to the proximal physis if possible). Bend the protruding fibular wire at its distal end and curve it around the lateral malleolus so it can be buried.

Step 15: Tibia and fibula cortical bone burring: Burr the cortical bone on either side of the pseudarthrosis of the tibia and fibula. Especially, burr the lateral aspect of the tibia and the medial aspect of the fibula.

Step 16: Periosteal graft harvest and meshing: Release the leg tourniquet and proceed to the ipsilateral iliac crest, which was also prepped and draped free. Make an incision along the iliac crest. Dissect down to the external oblique muscles, which are partially peeled



Figure 3 i

Locking wire is bent on itself laterally and pulled back into tibia and then cut medially

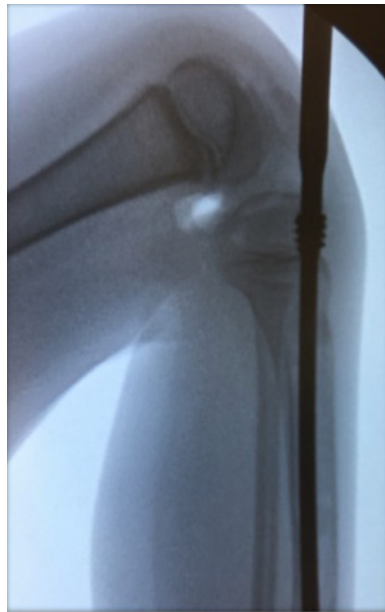


Figure 3 j

Female part of FD nail is screwed into the proximal epiphysis

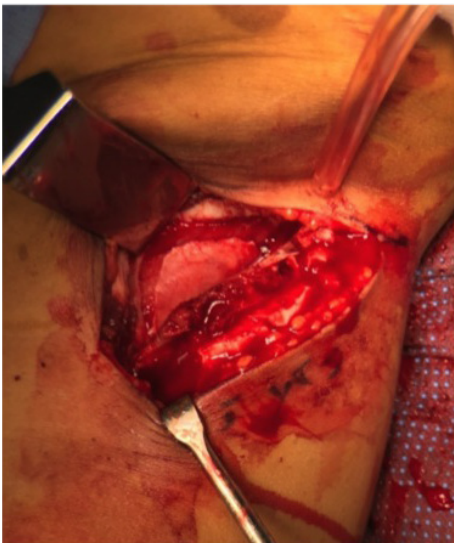


Figure 3 k

Periosteum on undersurface of iliacus muscle incised for harvest of periosteal graft

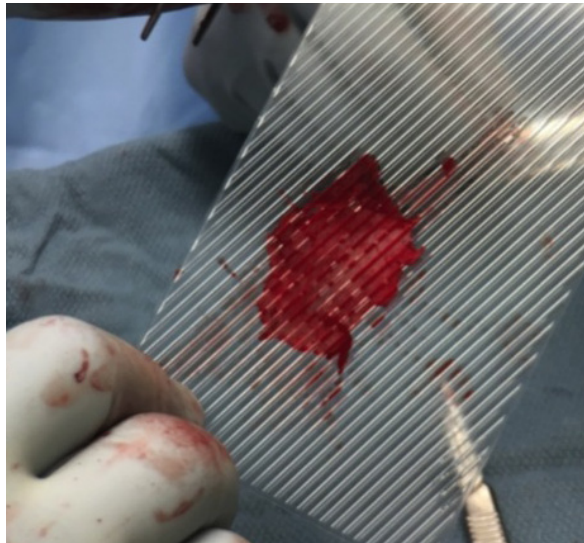


Figure 3 l

Periosteal graft meshed using skin graft mesher

medially with a cautery. Open the interval between the tensor fascia lata (TFL) and the sartorius staying on the TFL side to avoid the lateral femoral cutaneous nerve. Expose the anterior inferior iliac spine (AIIS) and the ridge between the anterior superior iliac spine (ASIS) and the AIIS. Split the apophysis from the AIIS to the ASIS and continue the split along the iliac crest at least until its most superior point. Peel the apophysis and the attached periosteum away from the ilium medially and laterally. On the medial side incise the periosteum of the undersurface of the iliacus muscle (Fig. 3k). Incise it in a rectangular fashion to excise as large a piece of periosteum as possible. Dissect this periosteum from the muscle and then lay it on the plastic sheet used for meshing a skin graft (Fig. 3l). Mesh the periosteum in order to expand it.

Step 17: Tie two 4.0 sutures to the leading edge of the periosteum. Pass these sutures around the posterior aspect of the tibia and then pull the periosteum around the tibia. Make sure the cambium layer (layer that was previously facing the bone) is facing towards the bone. Once the periosteum is circumferentially around the tibia, suture its ends to each other to secure it in place (Fig. 3t).

Step 18: Iliac bone decancellousization (Figure 3m,n,o,p,q): Using a very sharp thin osteotome split the two tables of the ilium along their entire length. Extend this split from the ASIS to the AIIS. Carefully extend the split deeper and deeper into the ilium along its entire length. As the osteotome goes deeper between the tables it should head towards the supraacetabular region, triradiate cartilage, sciatic notch, posterior iliac crest and sacroiliac joint. Gradually widen the split as you proceed from anterior to posterior and from proximal to distal. The idea is not to perforate the cortical bone of the ilium, triradiate cartilage, hip joint, sciatic notch or SI joint. Curette the cancellous bone from between the tables of the ilium. The entire anterior and posterior iliac crest cancellous bone can be harvested without taking any of the cortical bone of the tables. There is a large amount of cancellous bone in the SA and triradiate cartilage regions. There is also a lot of cancellous bone around the sciatic notch and the SI joint regions. Even in a 12 month old, 15 cc of bone can be harvested. In older children 30-50 cc of bone can be harvested in this manner (Fig. 3r).

Step 19: Iliac crest backfill (Fig. 3s): Back fill the iliac crest with demineralized bone matrix if available. Close the iliac apophysis and suture back the external oblique muscles.

Step 20: Fasciotomy: Extend the anterior compartment fasciotomy proximally.

Step 21: BMP preparation: Prepare the BMP2 (Infuse, Medtronic, Memphis, TN) approximately 15 minutes before insertion. Insert one BMP2 sponge posterior to the tibia and the interosseous space.

Step 22: Autogenous cancellous bone graft insertion (Fig. 3u): Apply the autogenous cancellous bone graft overtop of this between the tibia and fibula extending proximal and distal to the pseudarthrosis sites of the tibia and fibula. Lay some bone medial, and anterior to the tibia. Check with the image intensifier that the bone graft is located in the desired position.

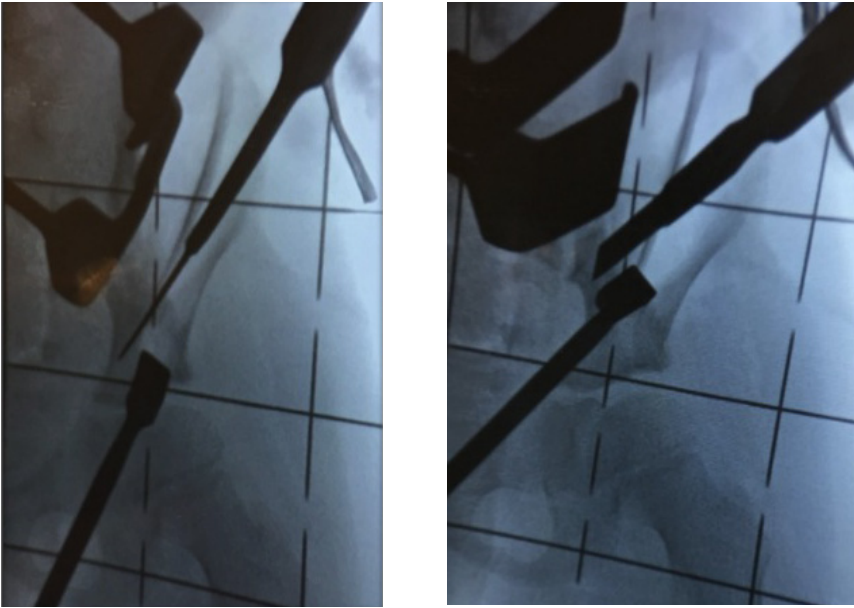


Figure 3 m, n

Iliac crest tables split using thin sharp osteotome down to dome, sacro-iliac notch and joint

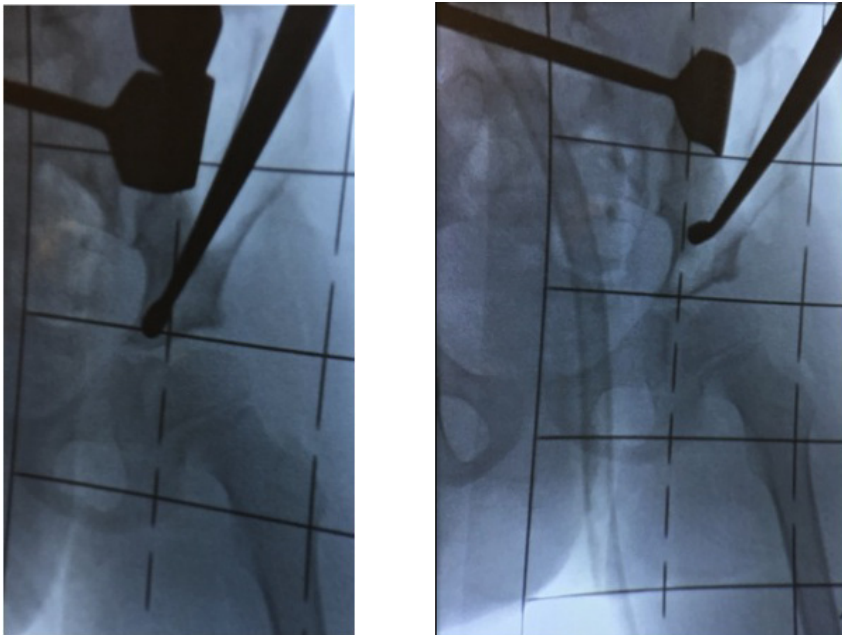


Figure 3 o, p

Decancellousization with curettes

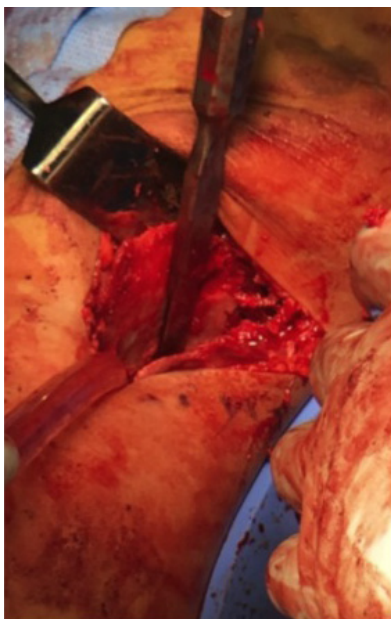


Figure 3 q

Clinical picture of split of iliac tables



Figure 3 r

40cc of bone harvested



Figure 3 s

Space between iliac tables filled with calcium sulphate/phosphate filler



Figure 3 t

Periosteal graft sutured in place around docking site

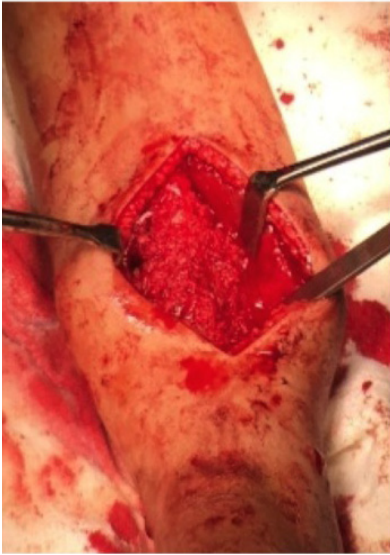


Figure 3 u

Cancellous bone inserted around tibia and between tibia and fibula

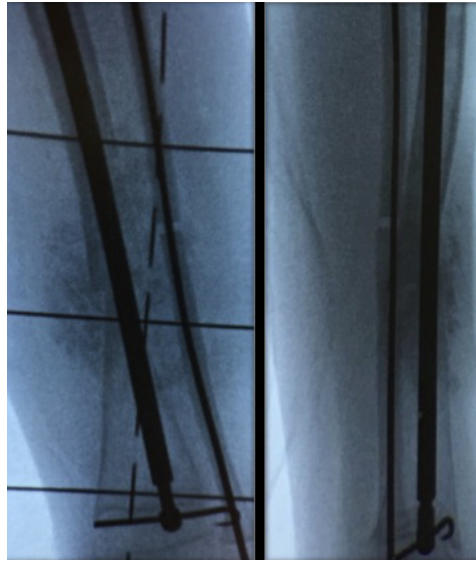


Figure 3 v

AP and lateral intraop fluoroscopy images showing cancellous bone surrounding tibia and between tibia and fibula



Figure 3 w, x

AP and lateral radiographs 12 weeks after surgery. A locking plate was used as an 'internal external fixator' to compress the bone ends and provide rotational stability. The tibia and fibula are already healed after only three months. The cross union between the tibia and fibula is already present.

Step 23: BMP insertion: Cover the bone graft with the remaining BMP2. The BMP2 should always be located between the soft tissues and the bone.

Step 24: Incision closure: Insert a hemovac drain and close the leg incision in layers. Similarly close the iliac apophysis and the iliac crest incision.

Step 25: External fixation application: If a plate was used in step 13, the operation is completed (Fig. 3x,w). If not, then apply a two ring Ilizarov apparatus to the leg. The threaded rods should be parallel to the tibia in both planes. Affix it to the tibia with two proximal and two distal counter-opposed olive wires. The bone ends are placed under compression. Wires do not need to be placed through the foot. A third empty ring is placed beneath the foot for weight bearing. An orthoplast splint is used to support the plantar aspect of the foot at 90 degrees by using Velcro straps to the external fixator. This last ring intentionally defunctions the foot so that no weight bearing occurs through the foot. Final radiographs should be obtained before leaving the operating room.

Postoperative care

The patient's incisions are checked two weeks after surgery. If a plate was used then a short leg cast non-walking cast is applied. Radiographs of the tibia and pelvis are obtained at 6 and 12 weeks after surgery. The tibia is usually united by 12-16 weeks after surgery. The tibio-fibular synostosis is also usually bridged with bone by 12 weeks after surgery. Whether a plate or a fixator is used, weight bearing is restricted for six weeks to allow the supra-acetabular bone to fill in. Once the cross union and tibia have united (usually between 3-5 months after surgery) the external fixator can be removed and a long leg-walking cast applied. A second zolidronic acid infusion is given at the time of fixtor removal. If a plate is used a second infusion is given between 3-4 months after surgery. Four to six weeks after fixator most of the swelling has subsided so that the cast can be removed and the leg measured for a custom brace. A knee-ankle-foot orthotic with a free knee and ankle hinge is prepared for the children under age six and a PTB total contact orthosis with an articulated ankle for the children over age six. As the patient gets older the length of the brace is reduced to an articulated AFO and then eventually to a gator brace (brace with malleolar flanges but no foot portion (usually after age 10). Brace wear at all times during the day including a separate water brace for swimming and water activities. The brace is taken off for bathing, sleep and physical therapy. Sports and other activities are permitted while wearing the brace.

The FD rod should be changed as needed to a larger diameter rod as the patient grows. Since the length of the bone doubles from age 3 in girls and 4 years old in boys until skeletal maturity, the telescopic rod has to be changed, at least twice before maturity. Hemi-epiphysiodesis is also performed if a valgus ankle or knee is present. The presence of the rod does not impede the use of a hemi-epiphysiodesis screw plate device.

► VALGUS OF THE ANKLE AND SHORTENING OF THE FIBULA

Valgus of the distal tibia is almost always associated with some proximal migration of the fibula. At the time of the initial repair of the CPT, if there is a significant proximal fibular migration, this can be adjusted surgically. This requires releasing the anterior and posterior distal tibio-fibular ligaments. Both can be released from the front. Some release of the interosseous membrane may also be needed. Once this is done the tibia can be relatively shortened to the fibula to relatively lengthen the fibula. The distal tibio-fibular syndesmosis can be fixed with a suture system such as the Ziptite (Biomet-Zimmer, Warsaw, IN) or the Titerope (Arthrex, Naples, FL).

Relative overgrowth of the fibula is a recognized complication of distal tibio-fibular synostosis after fracture.²⁴ This is related to the differential growth rate of the distal fibula to the distal tibia.²⁵ This is the subject of future study in CPT patients treated by cross union.

► ANTEROLATERAL BOWING (ALB) WITHOUT FRACTURE

The treatment of the unfractured anterolateral bowing is controversial. It is assumed that these represent a preCPT. The exception to this is ALB associated with a duplicated big toe with hallux varus. This type of ALB is benign and is not subject to fracture or pseudarthrosis.²⁶ More commonly however ALB without fracture is associated with NF or Fibrous dysplasia and is a precursor to CPT. The most accepted treatment is bracing.²⁷ Brace treatment has been shown to prevent fracture. The McFarland bypass graft has also been used in these situations to prevent fracture.²

Neither of these treatments prevents the secondary compensatory changes that occur with a chronic anterolateral bowing. These include: calcaneus ankle joint contracture, cavus foot deformity with verticalization of the body of the os calcis, weak push off, valgus ankle, lateral subluxation of the talus with proximal migration of the fibula, and leg length discrepancy.

To prevent these secondary changes, I prefer to osteotomize the tibia in patients with ALB without fracture. This approach is frowned upon because it is assumed that the risk of pseudarthrosis is too great. I treat ALB without fracture by the same protocol as CPT. Since I am able to get CPT to unite in all cases, then getting a preCPT case to unite after osteotomy should have the same outcome. The treatment protocol is identical with the only exception that there is no CPT and instead the surgeon performs the osteotomy at the apex of the angular deformity. Once this is done the rest of the treatment is the same as the Paley X-UNION protocol.

Meta-analysis of the Authors Results during the past 29 years:

Over the past 29 years, I have personally treated and followed 63 patients with congenital pseudarthrosis of the tibia. My results were published in two previous peer reviewed journal articles and in two book chapters. The data published in these articles and book chapters has been updated to include information about union and refracture rates. The data is divided into four different treatment groups. The different treatments have evolved over time adding elements to the treatment regiment that were believed to contribute to union and to reduce refracture.

Group 1: 1987-1994

- Ilizarov apparatus for compression-distraction and stabilization
- Bone grafting of CPT site in some cases.

Group 2: 1994-1997

- Ilizarov apparatus for compression-distraction and stabilization Rodding of tibia.
- Bone grafting of CPT site in some cases.

Group 3: 1997-2006

- Ilizarov apparatus for compression-distraction and stabilization
- Rodding of tibia and fibula.
- Resection of Periosteal Hamartoma
- Periosteal grafting of CPT site
- Bone grafting of CPT site

Group 4: 2007-2016 (Paley X-Union Protocol)

- Ilizarov apparatus for compression-distraction and stabilization
- Rodding of tibia and fibula.
- Resection of Periosteal Hamartoma
- Periosteal grafting of CPT site
- Bone grafting of CPT site of tibia and fibula
- Cross Union of tibia to fibula using bone graft
- Zolidronic Acid Treatment prior to surgery and at time of fixator removal
- BMP-2 insertion

The results of these treatments are summarized in Table 1.

Table 1

Treatment Group	Union %	Refracture %
Group 1 n=22	100	68
Group 2 n=12	100	29
Group 3 n=12	100	75
Group 4 n=17	100	0
Total n= 63		

OBTAINING union was achieved in all cases. Despite this the refractures seen in Groups 1-3 indicate that the problem is MAINTAINING union. (All refractruers in this series were treated and union was achieved. Some went on to refracture again and were again retreated and union achieved. To the best of my knowledge 62/63 patients remain united; 1 refractured tibia patient opted for an amputation by another surgeon).

There are four factors that are associated with poorer prognosis: 1) lower age at treatment; 2) previous failed treatment; 3) neurofibromatosis; 4) increased followup

	Mean Age (yrs) at treatment	% previous failed treatment	NF %	Followup (yrs) average
Group 1	8	39	70	8
Group 2	8	35	55	6
Group 3	5	25	67	6
Group 4	4	41	59	3

Compared to Group 1-3, Group 4 has a tendency for a lower mean age at treatment which is a negative prognostic factor. Group 4 also has a shorter average followup than the other groups. None of these factors can explain the precipitous drop in refractures seen in Group 4 compared to the other groups. A similar finding was noted by Choi et al and will be discussed later. The difference between the treatment in Groups 1-3 and Group 4 is the addition of a cross union and the use of BMP and ZA. BMP and ZA certainly help in acheiving union and cross union and may even speed up this process. Their impact however is short lived and they would not be expected to impart any long lasting protection from refracture. The cross union, on the other hand remains in place and augments the union. The cross union creates a much wider cross sectional area of bone at the CPT site making refracture much less likely. Combined with rodding of the two bones, the cross union produces an incredibly strong construct to resist fracture. Therefore it is safe to conclude that it is the addition of the cross union that caused this precipitous drop in

refracture rate. The ZA acid treatment prior to the bone graft harvest makes the likelihood of union and cross union greater and the BMP may account for the speed of achieving union in only 3-4 months.

► DISCUSSION

The natural history of CPT is recalcitrant nonunion, atrophy of the bone and the leg, progressive LLD and deformity, and recurrent refracture even after union is achieved in surgery [3,4,28,29,30]. The primary objective of treatment for CPT is to *obtain* union. The secondary objective is to *maintain* union. In addition, many associated deformities of length and angulation should be addressed in the comprehensive management of CPT. Therefore, unless all patients have reached skeletal maturity, the refracture rate reported is always lower than actual.^{3,4,30}

The main surgical options for treatment of CPT are vascularized fibular grafting, IM stabilization, external fixation with a circular frame, and amputation.^{21,22,31-37} Electric stimulation has also been studied.^{17,38}

Paley et al²¹ presented a report of 15 patients who had 16 tibiae with congenital pseudarthrosis. The mean patient age was 8 years, the rate of union was 94% in 15 patients with Ilizarov frames, refracture occurred in five tibiae (31%), and the mean follow-up duration was 4 years.

Boero et al³⁹ presented a report of 21 patients with neurofibromatosis treated with Ilizarov frames. The mean patient age was 8.8 years. The primary union rate was achieved in 17 of 21 (81%) patients. Refracture occurred in four of the 17 patients (19%), and the minimum followup duration was 2 years.

The European Paediatric Orthopaedic Society (EPOS) multicenter study²² of 340 patients with CPT reported a 75% healing rate achieved with Ilizarov external fixation and recommended the use of prophylactic IM rodding to prevent refracture.

In a series of 17 tibiae with CPT treated by Paley and Herzenberg, half of which were followed up to skeletal maturity, the mean patient age was 8 years, union was obtained in 100% of the patients, and refracture occurred in 68% when the Ilizarov device without IM rodding was used.¹⁸ When IM rodding was combined with external fixation, the refracture rate dropped to 29%.

Ohnishi et al⁴⁰ reported 73 cases that were treated with different treatment protocols: 26 with Ilizarov fixation, 25 with vascularized fibular grafting, seven with the combination of the previous two techniques, six with IM rodding combined with free bone grafting, five with plating and grafting, and the remaining four with different treatment protocols. The average patient age was 5 years. Union was achieved in all patients treated with Ilizarov fixation (four experienced refracture), 22 of 25 (88%) patients treated with free vascularized fibular grafting (one experienced refracture), and all patients treated with both fibular grafting and Ilizarov fixation.

IM rodding is an alternative treatment option to achieve and maintain union, although the reported results are variable. Joseph and Mathew⁴¹ reported 14 skeletally immature patients treated with IM rodding and double onlay autogenous bone grafting from the opposite tibia. The mean patient age was 4.5 years, the union rate was 86%, the mean followup duration was 3 years, and the refracture rate was 21% (three of 14).

Johnston⁴² reported on 23 patients treated with different techniques of IM rodding and grafting. The mean patient age was 2 years 4 months, the mean followup duration was 9 years, the primary union rate was 87%, and 13% had persistent nonunion and bad outcomes. The author noted that two important factors for the best outcome for patients with CPT were perfect limb alignment and the use of IM rods to achieve union, prevent refracture, and maintain alignment.

Kim and Weinstein⁴³ reported on 11 patients with 12 tibiae with congenital pseudarthrosis treated with IM rodding and free bone grafting. The mean patient age at the time of the index operation was 2.5 years. Four of the 11 patients healed after the primary index operation. Two of the four experienced refracture; one healed with a long lower limb cast, and the other healed after the index operation was repeated. The other seven did not heal after the index operation. Four of them achieved healing after undergoing multiple surgical procedures (one required free vascularized fibular grafting, and three required repeated IM rodding and grafting; one of the three had nonunion, one needed Syme amputation, and one had a failed Sofield procedure). Healing could not be achieved in the other three patients (two underwent below-knee amputation, and one had persistent nonunion at the latest followup visit). Kim concluded that IM rodding provides more predictable results in cases of late-onset pseudarthrosis.

Dobbs et al^{31,32} reported the long-term followup (mean followup duration, 14.2 years) of 21 patients with CPT (mean patient age, 5.1 years) treated with IM rodding and bone grafting. The primary union rate was 86% (18 patients), and three patients required additional bone grafting to achieve union. Twelve patients (57%) experienced refracture, and five (24%) required amputation.

Free vascularized fibular grafting had been described by several authors as a good option for achieving union in patients with CPT, although it is associated with many drawbacks, including nonunion, refracture, and recurrent nonunion at one site of the graft end.^{33,44-46} Angular deformity of the affected tibia (valgus or anterior bowing) has been reported. The deformities usually are progressive and require further treatment.⁴⁵⁻⁴⁷ Donor site morbidity, such as progressive ankle valgus with proximal migration of the distal fibula, is another problem associated with vascularized fibular grafting.⁴⁵⁻⁴⁷ The tibiofibular synostosis can only delay but not prevent ankle valgus.⁴⁵

Weiland et al⁴⁶ reported 19 patients with a 95% union rate. Initial failure to achieve union occurred in 26% (five of 19 patients), and those patients required secondary procedures to achieve union (four healed and one underwent amputation).

Gilbert⁴⁴ reported the long-term followup of 29 patients who had CPT treated with microvascular fibular grafting, all of whom had reached skeletal maturity. The union rate was 94% with a mean healing time of 6 months. The mean patient age at the time of the index operation was 5.5 years, the refracture rate was 14%, and the recurrence rate was 7%. Donor site morbidity occurred in 24%, tibial deformity (valgus and anterior bowing) occurred in 24%, progressive LLD occurred in 7%, and no amputation was recorded.

The EPOS study^{10,36} reported a healing rate of 61% (19 of 31 patients) for vascularized fibular transfer. Seven of the 19 healed patients required additional procedures, such as grafting, plating, or IM rodding. The remaining 12 healed after the primary treatment and did not require additional surgery. Three patients (10%) required amputations, seven (23%) had not healed, and five (16%) experienced fracture of the transferred fibula.

Toh et al⁴⁸ reported seven cases of CPT treated with vascularized fibular graft, with a mean followup duration of 12.1 years. Casting or monolateral external fixation was used in the first cases; an Ilizarov fixator was used as a postoperative immobilization tool in one case. The author concluded that the best outcome can be achieved with combined vascularized fibular grafting and Ilizarov external fixation as a method of postoperative fixation.

El-Gamal et al³⁴ reported three cases of CPT treated with vascularized fibular grafting combined with Ilizarov fixation to distract the fibular graft to correct LLD with a single operation. They called it 'telescoping vascularized fibular graft'. The mean patient age was 9 years, and the mean followup duration was 2 years. Union was achieved in all cases. One patient experienced refracture, and another patient experienced ankle valgus of the affected site.

Amputation is an option in cases of CPT.^{35,37} Its incidence varies from series to series. McCarthy³⁷ noted that foot condition, number of operations, and severity of LLD are the factors that determine the need for amputation.

Pharmacologic therapeutic solutions for CPT recently have become available: BMP2, BMP7 and bisphosphonate therapy (ZA).^{8,9,23} Lee et al⁸ reported five cases of CPT treated with BMP7 combined with corticocancellous allograft and IM rodding combined with external fixation. The mean patient age was 6 years, and the mean followup duration was 14 months. The authors concluded that the use of recombinant human BMP7 is not enough to overcome the poor healing environment associated with CPT. Little and colleagues^{31,49} used bisphosphonate (ZA) for patients with CPT to control the activity of osteoclasts to promote union. The bisphosphonate was given after bone graft harvest so that it could not protect the bone graft bone from resorption.

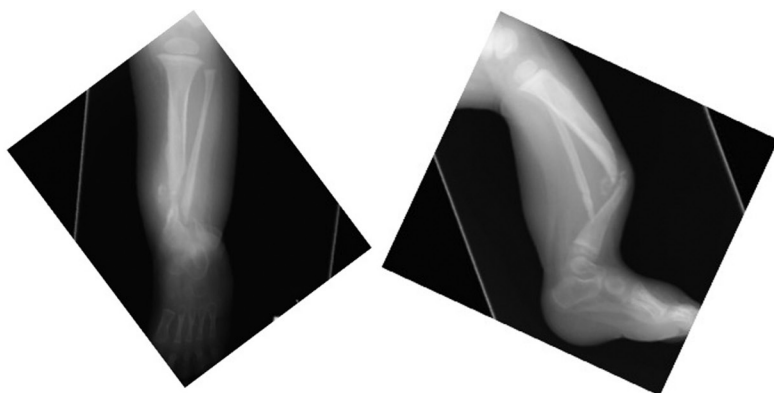
Thabet, Paley, Kocoaglu, et al¹⁹ conducted a retrospective study of 20 patients with CPT who were treated with periosteal grafting and bone grafting combined with IM rodding of the tibia and fibula and circular external fixation by the senior authors between 1997 and 2006 at two centers. The mean age at the index operation was 4.2 years (age range, 1-11.3

years). Eleven patients (55%) had neurofibromatosis, in seven patients (35%) the condition was idiopathic, and two patients (10%) had osteofibrous dysplasia. Twelve patients (60%) had no previous surgery, and eight patients (40%) had undergone at least one unsuccessful operation (range, 0-14). All patients had established pseudarthrosis. Union was achieved in all patients (100%). The mean time spent in external fixation was 5.2 months (range, 3-12 months). Limb lengthening was achieved in 12 patients. The mean lengthening amount was 2.5 cm (range, 0-7 cm); epiphysiodesis of the opposite side was performed in one patient.

Refracture occurred in eight patients: six experienced one refracture each, and two experienced two refractures each. Six of the eight patients with refracture had fibular pseudarthrosis. The mean time between the index operation and refracture was 2.3 years (range, 1-5.8 years), and the mean time between the index operation and second refracture was 4.7 years. The mean age at the index operation of patients who experienced refracture was 4 years (range, 1-7.3 years). The mean follow-up duration was 4.3 years (range, 2-10.7 years). All of the refractures were treated and all healed with surgery.

Choi et al, recommended creation of a cross union between the tibia and fibula for CPT cases where the fibula was broken but minimally proximally migrated. They converged the two fibula bone ends towards the two tibia bone ends in what they called a “4-in-1 Osteosynthesis”.⁵⁰ They used a cortico-cancellous sheet of the outer wall of the ilium combined with cancellous bone chips to achieve the cross union. They did not recommend this method when the fibula was intact or when the fibula was significantly proximally migrated. They reported 8 cases treated at a mean age of 6.3 years. All 8 united and developed a cross union to the fibula. There were no refractures at an average of 7.4 years (2.7-12.4). They compared this to a smaller group of 5 patients who had end-to-end repair of the tibia without crossunion. All 5 united but all 5 eventually refractured and required further treatment for the CPT. Choi et al, attributed the large cross section of the bone at the level of the cross union as the reason for no refractures. To quantitate this they measured what they called the relative cross sectional area (rCSA = area at the CPT site after union divided by area at the upper tibial physis). The rCSA was significantly lower in the non-synostosis group that all went to refracture 0.13 vs 0.27 in the synostosis group that did not refracture.⁵⁰

Paley reported his preliminary results using combined pharmacologic and surgical management with cross union (Figs. 4,5), which is herein referred to as the Paley X-UNION protocol, in 2012.⁵¹ Since that manuscript was written and submitted before the publication of the Choi et al article, I was not aware of the Choi et al method which predates my own conclusion and technique to perform a cross union. Although I reached this idea independently of Choi et al’s publication, Choi et al deserve credit for first conceiving of this idea. They began performing their cross union technique in 1999, while I did not start doing this until 2007. The Choi et al technique differs from the Paley technique in several ways. In the Paley cross union technique the tibia and fibula are both rodded straight, keeping the tibia and fibula their normal distance apart without converging them towards

**Figure 4 a, b**

AP and lateral radiographs of 1 year old girl with congenital pseudarthrosis tibia and fibula with severe anterolateral bow and NF

**Figure 4 c**

Intraoperative photos showing bone ends after hamartomatous resection (left) and after rodding (right)

**Figure 4 d**

Intraoperative radiographs showing large amount of autogenous bone graft around tibia and between tibia and fibula and external fixation

**Figure 4 e**

Two year followup radiographs showing excellent cross union and healing of CPT of both bones. Ample growth with telescoping of FD nail has occurred. The distal end of the rod is pulling through the distal physis. This occurs when the telescopic nail sticks and does not telescope further

**Figure 4 f**

Three year followup. FD rod exchanged



Figure 5 a,b
AP and lateral radiographs of a six year old boy with very distal CPT tibia and fibula and NF

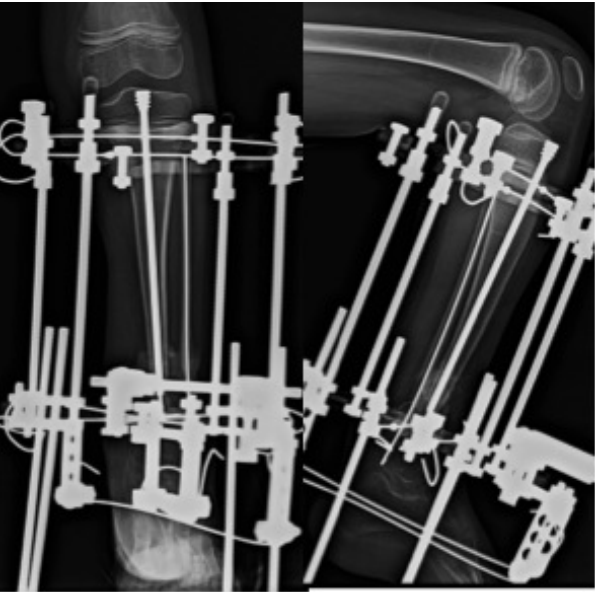
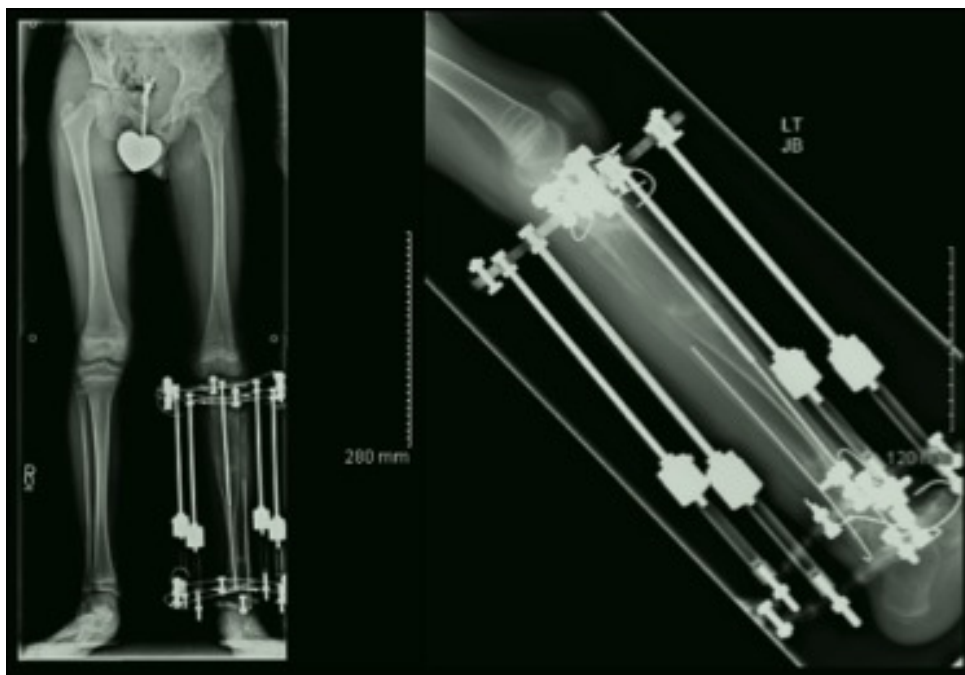


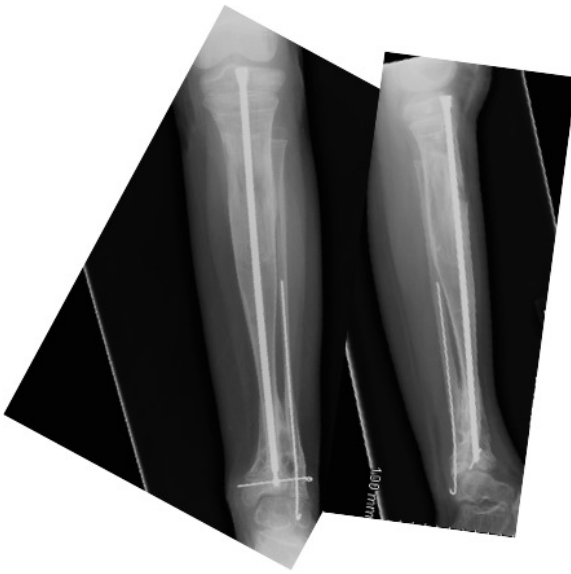
Figure 5 c
One month post surgery AP and lateral radiographs

**Figure 5 d**

Three months after surgery the external fixator was removed. There is a successful union of the CPTs and cross union between tibia and fibula

**Figure 5 e**

Two years later, 8cm lengthening of the tibia through a proximal osteotomy using a ring fixator

**Figure 5 f**

AP and lateral radiographs after fixator removal with exchange rodding, showing excellent consolidation of the regenerate bone and maintenance of the cross union

**Figure 5 g**

Standing radiograph after lengthening showing near equalization of limb lengths

each other. This results in almost twice as large a cross sectional area of healing (see below). The two authors also use different techniques for autogenous bone graft harvesting. In the Paley technique only cancellous bone is harvested and used. In Choi et al a sheet of cortico-cancellous bone is harvested and used. Paley also uses ZA and BMP both of which were not used in Choi et al. Obviously creation of a cross union can be achieved in more than one way. Paley et al recently reported the results of 17 CPTs treated using the Paley X-UNION protocol.⁵² Union was achieved in all cases and there were no refractures. The average follow-up was 3.7 years ranging up to 9 years. The average age at treatment was 4.5 years with patients as young as 11 months at the time of treatment. Union and cross union were achieved in all cases at an average of 4 ± 0.6 months. The rCSA was a mean of 0.46 ± 0.14 . This rCSA is significantly higher than that reported by Choi et al. This is not surprising since the fibula and tibia in the Paley protocol are not converged as in the “4 in 1” Choi et al technique.

Combining BMP and bisphosphonate treatment in clinical practice is a useful adjunct as was shown in the animal model.²³ In a review of CPT, Johnston and Birch⁵³ advocated using BMP as an adjuvant treatment in all primary and recalcitrant cases. Despite optimism with the use of BMP, one must also consider theoretical risk of tumorigenesis because BMP stimulates the RAS pathway, which is also a tumor pathway. Patients with CPT have a propensity for both benign and malignant tumors. Although there has never been a report of such a complication, it should be discussed with patients since rhBMP is not FDA-approved for children or for CPT. Its use in CPT is considered off label.

The Paley method of combined pharmacologic-surgical treatment is a “kitchen sink” approach to management of this potentially devastating problem. It optimizes the mechanical³⁰ and biologic environment for the CPT. It is impossible to specifically identify which factor is more important for the healing of CPT. The meta-analysis reported above and the rCSA between the synostosis and control group reported by Choi et al both suggest that the cross union is the most important factor preventing refracture. As newer pharmacologic therapeutics and better understanding of the pathoetiology of this disease occur, the combined pharmacologic surgical technique will morph to include newer technologies and therapeutics. Meanwhile the combination treatment; hamartoma resection, periosteal grafting, bone grafting, internal rodding, external fixation, tibio-fibular cross union, BMP and bisphosphonate pharmacologic manipulation are the best current combination treatment for CPT.

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Key Learning Points

- CPT is a periosteal disease, which produces low BMP from the bone cells and has increased number of osteoclasts in the surrounding periosteum. As a consequence, the use of BMP to stimulate bone healing and zolidronic acid to decrease osteoclasts is synergistic and complimentary to healing.
- Creating a cross union increases the cross sectional diameter of the bone and makes refracture almost impossible.
- Intramedullary fixation is essential to help obtain and maintain union.
- Decancellousization of the ilium is a new and essential technique to be able to harvest a large enough volume of autogenous cancellous bone.
- The results of the Paley X-UNION technique yield 100% union and no refractures to date.

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