ACUMED®

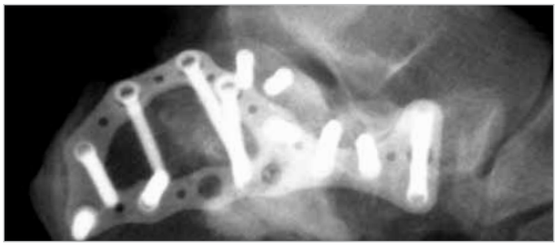
Innovative Solutions

CALLOS®

Calcium Phosphate Cement

Callos® Calcium Phosphate Cement

Since 1988, Acumed has been designing solutions for the demanding situations facing orthopaedic surgeons, hospitals and their patients. Our strategy has been to know the indication, design a solution to fit and deliver quality products and instrumentation.



Orthopaedic technology is constantly evolving due to the continuous improvement of fracture fixation and rehabilitation methods. Acumed strives to provide solutions that contribute to the advancement of new techniques and address the issues with current fixation procedures.

Acumed is pleased to offer the Callos Calcium Phosphate Bone Void Filler Cement in conjunction with innovative implants and instrumentation for the upper and lower extremities. With its many unique features and biomechanical properties, Callos contributes to Acumed's goal of improving fixation methods to ultimately provide the best possible outcome for the patient.

Key Indications Include:

- Tibial Plateau fractures
- Distal Radius fractures
- Calcaneal fractures
- Proximal Humerus fractures
- Backfill after bone graft harvesting
- Tumors and cysts

Callos is a next generation calcium phosphate cement indicated for filling bony defects in cancellous bone. This unique biologic cement provides immediate high compressive support where host bone has been compromised.

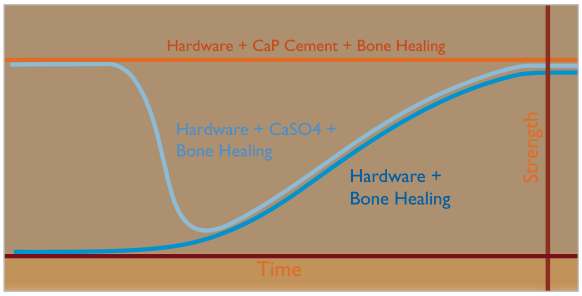
A scaffold is created to allow bony ingrowth to occur through a cell-mediated remodeling process. Host bone will replace Callos along with adjacent cancellous bone. Callos exhibits high compressive and tensile strength throughout the remodeling process.

Callos Impact® will permit drilling and hardware insertion in just 6 minutes, Callos Inject® will permit drilling and hardware insertion in 10 minutes.

Drillable Osteoconductive Scaffold:

Callos calcium phosphate cement provides a stable, secure and drillable osteoconductive scaffold to facilitate bony ingrowth and allows hardware to be placed.

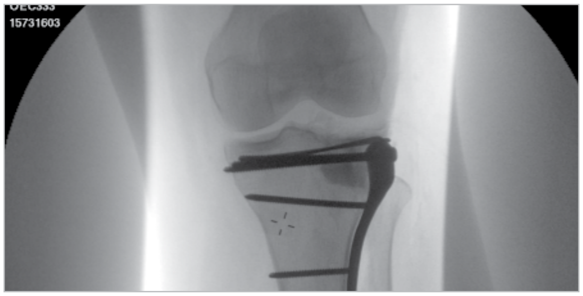
Callos remodels along with natural bone and can be drilled to allow adjacent hardware placement for both immediate and continuous strength. Improved tensile and flexural strength and greater fracture toughness over first generation calcium phosphate cements allow Callos Impact to accept hardware as early as 6 minutes after implantation.



Bone healing with CaP cement(orange line), CaSO4(light blue line), No Cement(dark blue line).

Ease of use:

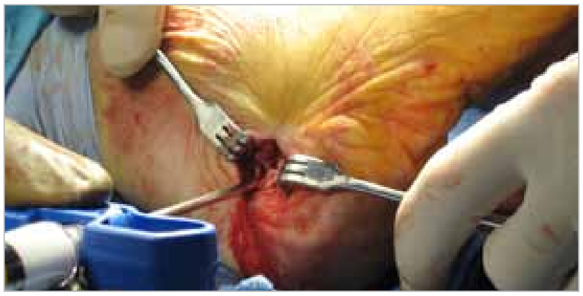
Following simple preparation instructions, the Callos Disposable Mixing and Delivery System is easy-to-use and results in a consistent mix every time. Unlike some other calcium phosphate cements, Callos sets quickly in an aqueous environment. Callos can be manipulated post-implantation, giving the surgeon an opportunity to refine their reconstruction.



Tibia Plateau with optimal harware and Callos® placement

Experience:

Acumed's next generation calcium phosphate bone void filler cement, Callos has been developed by a team of biochemists and material scientists with over 20 years of experience with calcium phosphates. For bony voids and defects in cancellous bone, the Callos team has again brought to bear its expertise in technology and chemistry to improve Acumed's unique biologic cement.



Callos being injected percutaneously.

Features of Impact and Inject:

- High Strength
- Biocompatible
- Moldable or Injectable
- Fast-setting
- Sets in a wet environment at body temperature
- Permits drilling and hardware insertion

Impact Contents:

- Callos Mixer
- Spatula
- Callos Powder and Liquid Set

Inject Contents:

- Callos Mixer
- Plunger
- Syringe and Cannula
- Callos Powder and Liquid Set

Drillable Osteoconductive Scaffold

Immediate post-op

1 year post-op

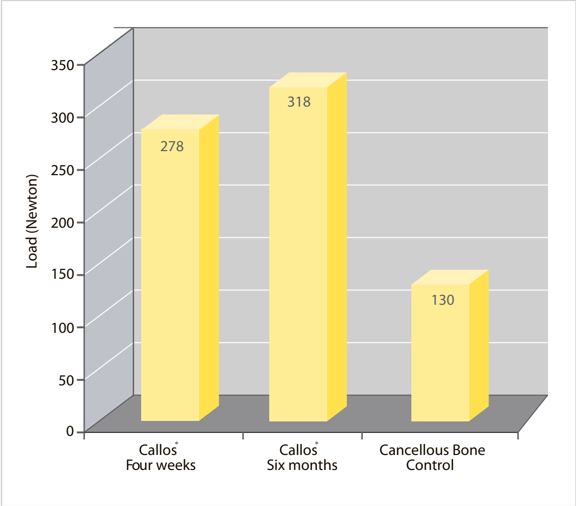


Figure 1. *Callos maintaining strength over time.*

Bone remodeling is the process whereby bone healing occurs through removal of old bone and replacement with new bone.

Callos is similar in composition to the mineral phase of bone. A calcium phosphate starting powder is reacted with liquid and undergoes a chemical reaction to form low crystalline hydroxyapatite, which hardens in vivo to create an osteoconductive scaffold that allows bony ingrowth through the same process as the patient's natural bone remodeling.

Calcium phosphate cement is optimal as a filler for metaphyseal defects due to its high mechanical strength and ability to maintain that strength throughout the healing process.

Callos is remodeled through a cell mediated process, providing immediate and long term strength.[1]

A biomechanical study comparing strength maintenance over time for both cancellous bone and Callos found cancellous bone to withstand 130N of compressive loading, while Callos withstood 278N of compressive loading four weeks post-implantation, and 318N six months later. Callos is stronger than cancellous bone and is able to maintain excellent strength over time (Figure 1).

Callos can be drilled and used together with hardware which is an excellent means of treating periarticular fractures. Callos is an excellent option for better screw purchase in osteoporotic bone – inserting a screw into Callos during the initial setting time allows the screw threads and Callos to create a rough interface by interdigitating and resisting screw backout post-setting.

Callos is radiopaque and is visible under flouroscopy to allow proper placement of hardware and to ensure the cancellous defect has been completely filled.

Callos should not be drilled with a K-wire. A fluted drill tip is needed to ensure optimum results.

Callos Impact can accept hardware after setting time of 6 minutes in patients body, and Callos Inject can accept hardware after setting time of 10 minutes in the patients body.

Ease of Use

The viscoelastic properties of Callos gives excellent options through two product lines; Inject and Impact. Callos is easy to mix, with Inject being highly flowable versus Impact, which is a more putty-like product. Both variations set very quickly. Impact has a 4-minute setting time; Inject has a 6-minute setting time.

Unlike first generation calcium phosphate cements, Callos does not "wash out" and is designed to set quickly in a warm, aqueous environment.

Callos can be manipulated post-implantation allowing for refinement of the reconstruction of the bone.

Callos is isothermic and non-toxic. Although no adverse reactions should occur in the soft tissues or joint space, extrusion of Callos into these areas should be minimized.[1,13,14] The body will absorb excess in the same manner as bone dust.

The new Callos Mixing and Delivery System relies on a hand-crank system for mixing the powder and liquid resulting in a consistent cement mix in one minute. Callos Inject adds an easy-to-use plunger for extruding Callos Inject directly into the syringe, while Callos Impact can be scooped out with the provided spatula.

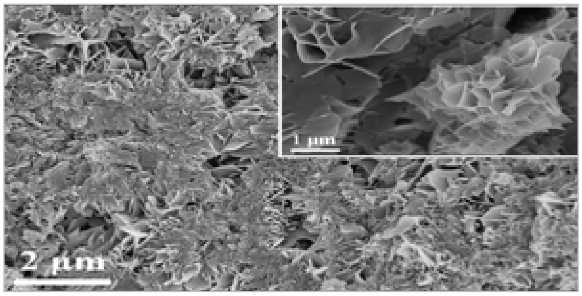
Callos Mixing and Delivery System

Experience

Developed by a team with over 20 years of experience with calcium phosphates, Callos is a unique, second-generation bone void filler with improved handling and ease of use.

The Callos team of biochemists and material scientists has developed a calcium phosphate cement for high performance in the body – Callos hardens quickly, does not wash away and is strong enough for drilling to support adjacent hardware.

The Callos team continues to improve performance, handling, mechanical and biological properties of Callos for the use as a superior bone void filler with immediate, high compressive strength.



Callos cured 1 day; Scanned Electron Microscope image.

Total Arthroplasty with Callos placed under tibial tray.

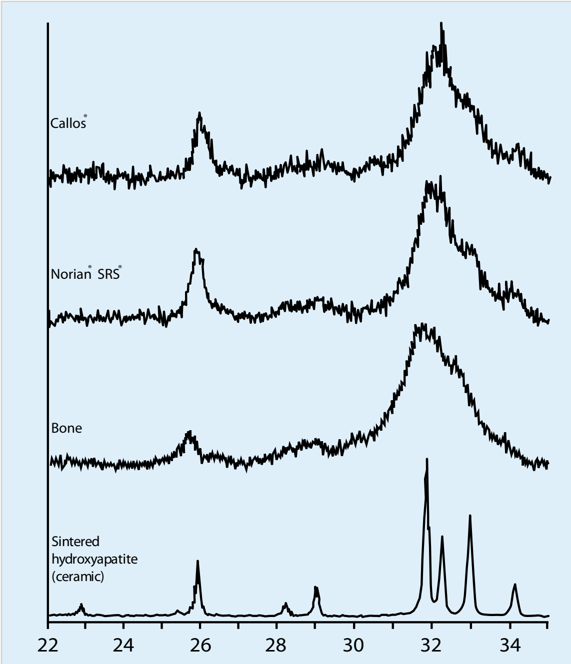


***Figure 1.** XRD patterns for Callos®, Norian®SRS®, bone and sintered hydroxyapatite. Callos and Norian SRS were both explanted and analyzed following four weeks in vivo implantation.*

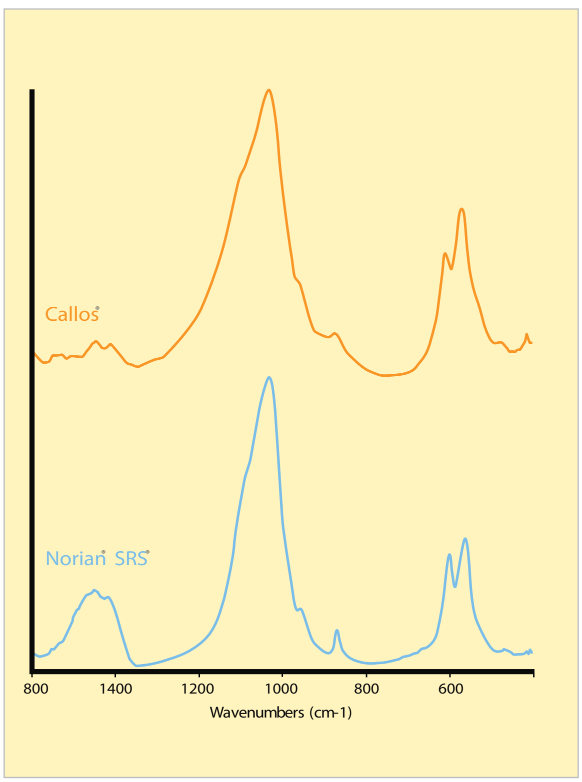


***Figure 2.** The Fourier Transform Infrared (FTIR) spectra for Callos® and Norian® SRS® show that both form carbonated hydroxyapatite in vivo, similar to the native mineral phase of bone. Callos and Norian SRS were both explanted and analyzed following four weeks in vivo implantation.*

X-ray diffraction (XRD) allows identification of the mineral phase of materials. Figure 1 illustrates the XRD patterns for Callos®, Norian® SRS®, bone and sintered hydroxyapatite (ceramic). The diffraction pattern of the Callos and Norian SRS materials are considerably broader than the sintered hydroxyapatite material and more closely resemble the diffraction pattern of bone due to their similar crystallinity.

Fourier Transform Infrared Spectroscopy (FTIR) is used to evaluate additional aspects of the crystallographic and chemical make-up of the implant. Both Callos and Norian SRS are poorly crystalline apatites, similar to the native mineral phase of bone (Figure 2). These FTIR spectra indicate that they share similar characteristic differences from "ceramic" or sintered hydroxyapatite in that they incorporate carbonate and acidic phosphate groups with their crystalline structure, leading to their poor crystallinity and enhanced solubility relative to highly crystalline 'ceramic' or sintered hydroxyapatite calcium phosphate.

The relative solubility of calcium phosphate bone void fillers was measured at 37°C in a physiologic solution with a pH=7.4. Calcium values begin to level off to an apparent equilibrium value of about 11 ppm after 5 days for Norian SRS and 9 ppm for Callos. These values are similar to those published previously for poorly crystalline apatite materials with similar chemical compositions and crystallographic structures.[1,2] The solubility curves for Callos® and Norian® SRS® show similar solubilities in vitro, which reflects their chemical and crystallographic similarities. Based on their similar in vitro solubility and dissolution rates at physiologic temperature and pH, Norian SRS and Callos are anticipated to have similar in vivo stability and remodeling rates.

Calcium sulfate (gypsum) or Plaster-of-Paris could not be plotted on this curve because its solubility is many orders of magnitude higher. This is why gypsum simply dissolves (autodegrades) rapidly in vivo, leaving a void before bone can infill a defect.[3] The promotionally advertised initial mechanical strength of Plaster-of-Paris cements is clinically irrelevant because they dissolve so rapidly in vivo. Strength is lost exponentially within a very short period of time, even though the radiographic disappearance of gypsum appears linear, giving a false sense that it remains mechanically intact.

Histological analysis demonstrated that Callos® is highly biocompatible and osteoconductive. Figure 3 shows histological analysis following four and six weeks in vivo and showed extensive bone apposition with no adverse tissue reaction. Normal bone remodeling by localized osteoclastic, cell-mediated resorption coupled with new bone formation within the implanted area was a consistent finding in areas implanted with Callos.

Over the last decade, reports in peer-reviewed literature and results from the above study have demonstrated that calcium phosphate cements remodel via osteoclastic cell-mediated resorption coupled with new bone formation.[4,5,6,7,8,9] It is important to note, that the use of standard radiographic imaging is limited in its capacity to show the progress of remodeling. A clinical radiograph takes a 3-D structure and produces a 2-D image. Figure 4 illustrates the "stacking" effect, which results during radiographic analysis of a 3-D structure. The 2-D image, which is produced by radiographic means, shows only the localized areas of sections that have not remodeled, represented as black boxes. These 'black box' areas need only be about 5-10mm in thickness to appear radio-opaque on a clinical x-ray.

Figures 5A and 5B are low power back-scattered scanning electron micrographs of tibial plateau sections from an in vivo canine study at 4.5 years from the same animal. 5A shows complete remodeling of the calcium phosphate cement, yet 5B, a different cross-section of the same sample, shows areas still comprised of cement. The radiograph, 5C, taken prior to sectioning the proximal tibia, illustrates the "stacking" effect seen when a 2-D image is produced from a 3-D structure. Although the micrographs show extensive remodeling, standard clinical radiographic analysis continues to show the presence of cement even at minimal levels and is not an effective means of measuring the extent of Callos cement remodeling.

Figure 6 illustrates the limitations of simple radiographic analysis for accurate follow-up evaluation and interpretation of osteoclastic cell-mediated remodeling and revascularization of the implanted area. Callos® was injected into cylindrical samples covering a range of thicknesses from 30mm down to 2mm and cured in vitro.

These samples were then x-rayed using standard radiographic technique for a distal radius fracture (54 Kv @ 7mA). The resulting radiograph highlights that one cannot easily distinguish the difference between cement bodies over 10-20mm in thickness. This shows that even with a significant decrease in the amount of the Callos implant, it is difficult to see any radiographic change, that is assuming no resorption and replacement by bone. With the added effects of remodeling native bone, bare implants alone show little evidence of radiographic significance as the implant remodels. As a result, especially in a clinical radiograph where both bone cement and new bone are present, the additive effect of the cement and bone render the radiograph completely radiopaque.

This misinterpretation in radiographic analysis has lead to the false interpretation that calcium phosphate cements are not remodeled even though all the histologic evidence demonstrates that they become completely replaced by bone in a mechanical stress-directed fashion.[4,5,6,7,8,9]

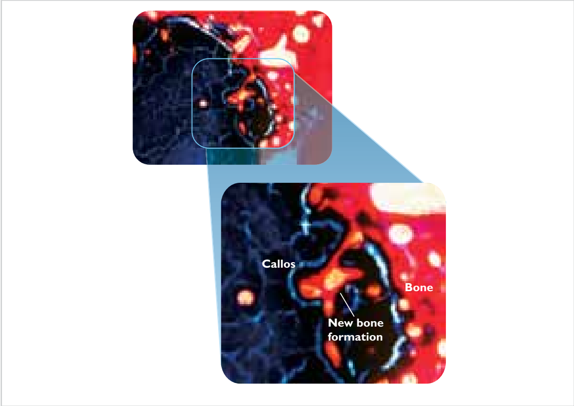


Figure 3. *The remodeling process over a one year period. Because Callos remodels at the same rate as the adjacent bone, both immediate and continuous postoperative strength are maintained.*

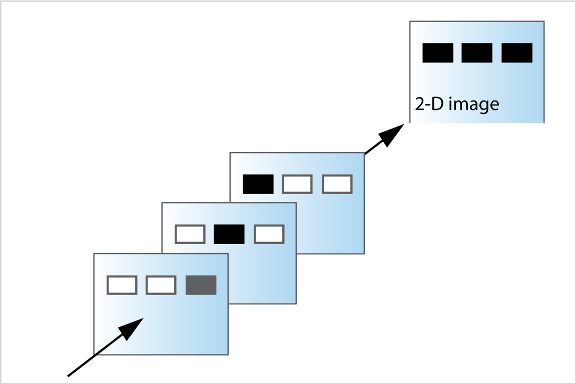


Figure 4. *The white blocks are areas that have completely remodeled and the black blocks are areas not remodeled.*

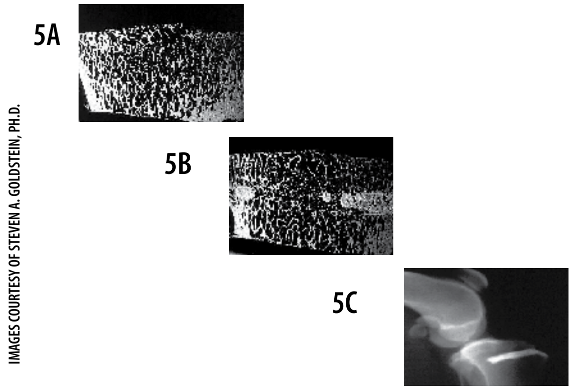


Figure 5. *Electron micrographs of tibial plateau samples.*

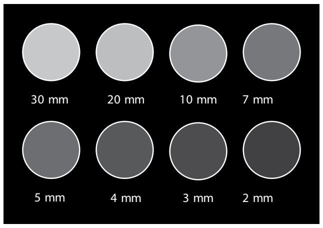
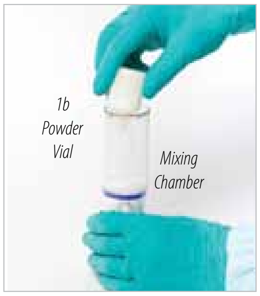
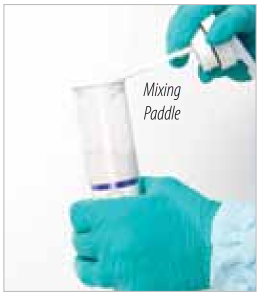


Figure 6. *Radiograph samples in the following thicknesses: 30mm, 20mm, 10mm, 7mm, 5mm, 4mm, 3mm, and 2mm.*

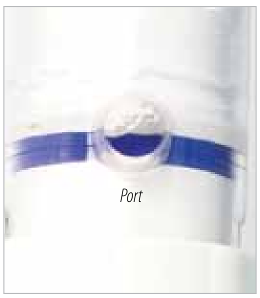
Callos Inject® Mixing and Delivery System Instructions



1
- Unscrew top from the mixer and pour Callos liquid FIRST into the mixing chamber.
- Pour Callos powder into the mixing chamber.



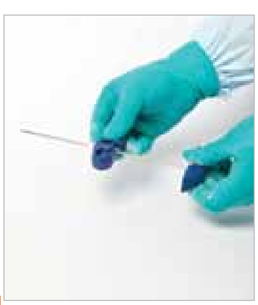
2
- Screw top back on the mixer and rotate the handle briskly in a clockwise direction for one minute.
- Remove top from mixer and scrape the cement on the mixing paddle back into the mixer.



3
- Rotate base of mixer all the way down.
- The base should stop with half of the exit port visible.
- Insert plinger and rotate down until cement starts extruding out of port.

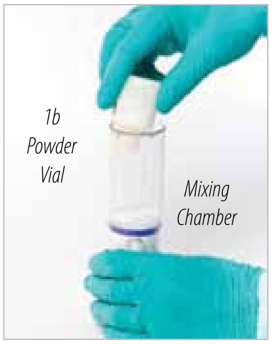
4
- Remove cap from syringe.
- Attach syringe to port on mixer.

5
- Rotate plunger down to extrude cement into syringe.
- Remove syringe from port and reattach cap.



6
- Remove trocar from cannula.
- Attach cannula to syringe and inject Callos.

1
- Unscrew top from the mixer and pour Callos liquid FIRST into the mixing chamber.
- Pour Callos powder into the mixing chamber.

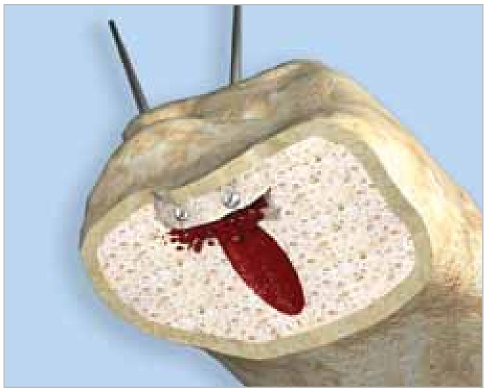


2
- Screw top back on the mixer and rotate the handle briskly in a clockwise direction for one minute.
- Remove top from mixer and scrape the cement on the mixing paddle back into the mixer.

3
- Use straight edge of the spatula, scoop cement out of mixer.

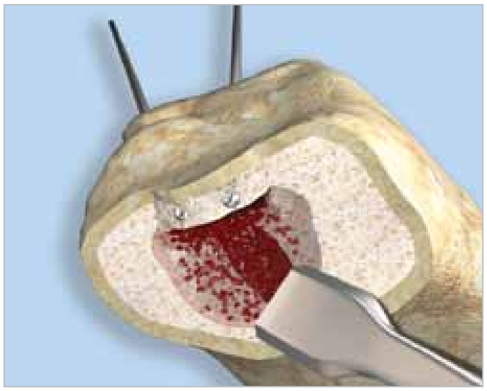
Basic Surgical Technique

The following two surgical techniques for Callos Bone Void Filler have been made available to the health care professional to illustrate the suggested treatment for the uncomplicated procedure. The first being a basic surgical technique for implanting Callos, the second, implantation of Callos in a Tibial Plateau fracture. Several surgeons, with years of experience in cementing of fractures, were consulted for the production of these techniques. Please review the timing charts in the back of the techniques to gain a fundamental understanding of the timing sequence for the implantation of Callos, which is essential for success.



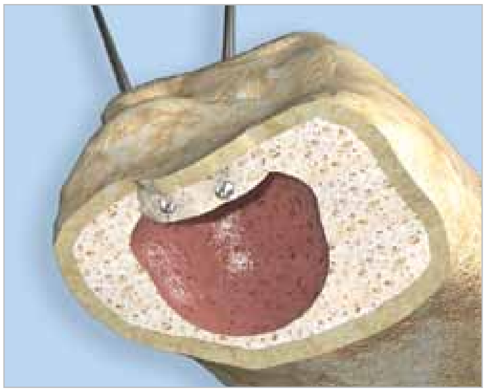
1 Fracture Assessment and Planning

Preoperatively assess the fracture's characteristics. Fractures with metaphyseal communition are the most appropriate for using Callos. Determine the approximate volume of Callos needed based on the predicted shape and location of the fracture void after reduction.



2 Reduction and Stabilization

Reduce and stabilize the intraarticular and extraarticular fracture fragments with provisional fixation. If desired, necessary hardware may be implanted at this time. Hardware may also be implanted following the implantation of Callos (Step 4). Visually verify fracture reduction with an image intensifier.



3 Void Preparation

Proper fracture reduction and void preparation are important to provide an optimal cement fill. Tools such as freer elevators or curved curettes should be used to examine the fracture void following reduction and fixation. This also delineates fracture characteristics and indicates the areas needing Callos.

To assure optimal fill, the fracture void should be irrigated and debrided to remove any clots, organized tissue and/or loose bone debris.

4 Implantation of Callos

A clear understanding of the timing sequence is necessary for the proper implantation of Callos (see timing chart). Verify fracture reduction and stabilization prior to the injection or impaction of Callos.

Mix Callos according to the instructions for use and implant into the fracture void via impaction or injection with fluroscopic guidance. Use an elevator to remove excess Callos from the fracture site and smooth the Callos to the surface with the cortical margins. Any extraosseus Callos in the soft tissues should be removed at this time.

1 Preoperative Radiographic Fracture Assessment and Planning

The surgeon obtains radiographs and other imaging techniques to determine the fracture characteristics. These include orthogonal and oblique radiographs of the knee, CT scan, 3-D reconstruction and MRI of the knee. A fracture with metaphyseal comminution is the most appropriate fracture type for Callos. During preoperative planning, the surgeon should determine the type of fixation necessary to repair the fracture and support the shear and tensile forces between the fracture fragments. Determine the approximate volume of Callos needed by predicting the shape and location of the fracture void after reduction.

Figure 1. Common split-depressed tibial plateau fracture.

2 Intraoperative Fracture Assessment and Stabilization

The fracture is assessed utilizing direct vision and fluoroscopic imaging. Manipulation and reduction of the fracture provides the opportunity to confirm or adjust the preoperative plan. Partial void preparation may be performed concurrently during the reduction. In selected cases, initial void preparation may be performed through the split fragment under direct visualization prior to provisional stabilization (see Step 3 Preparation of the Void). The articular surface is then reduced and provisionally stabilized. The reduction is verified visually and with the image intensifier.

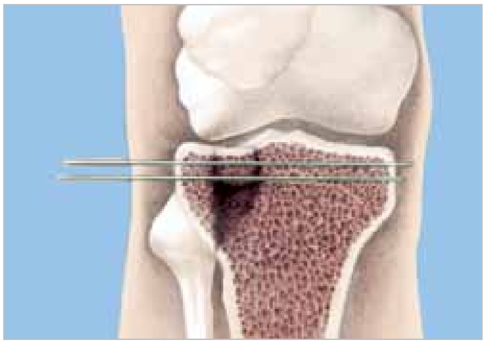


Figure 2. Placement of provisional hardware to aide in intra-operative fracture stabilization.

3 Void Preparation

Proper reduction and fracture void preparation are important to provide an optimal cement fill. This may be performed through a window, or as in this example, through the fracture line of the split portion of the fracture, which is usually an anterolateral split accessible between the tibial tuberosity and Gerde's Tubercle. Instruments such as elevators or curved curettes are used to explore the boundaries of the fracture void following reduction and stabilization. The cancellous bone at the periphery of the void is evaluated for structural integrity. If necessary, surgical preparation such as impaction of the compromised cancellous bone at the periphery is performed to provide a solid cement-to-bone interface.

Although Callos will displace blood and set within a bloody field, the post-reduction fracture void should be irrigated and debrided to remove clot, organized tissue and loose bone debris to allow for optimal fill.

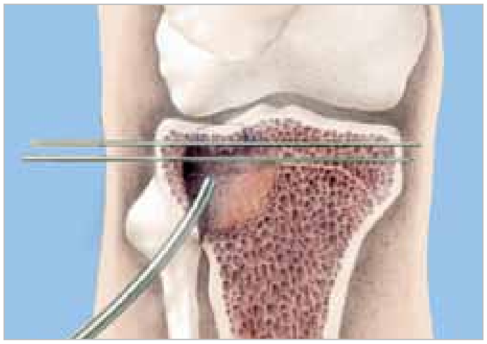


Figure 3. Proper void preparation of the post-reduction fracture void.

4 Implantation of Callos

A clear understanding of the timing sequence for Callos Inject and Impact relative to the estimated temperature of the fracture void is required for proper implantation (see timing chart on back). The surgeon may choose to apply the definitive hardware either before or after the implantation of Callos. If the fracture void is accessible, it is preferable to use Callos Impact and digitally impact the cement into the void, obtaining maximal void fill and local pressurization. After the hard setting of the cement, definitive hardware can be applied to the region. Final tightening of the screws can be achieved after additional cement setting in accordance with the timing chart. If the void is not accessible, and it is necessary to inject the cement into the void, then Callos Inject should be used. In this case it may be preferable to place the definitive hardware first, then inject the Callos Inject into the void under fluoroscopic guidance, obtaining maximal fill. Postoperative rehabilitation is based on many variables: the quality of the fracture reduction, adequate void filling, strength of the fracture construct, and the goals of both the surgeon and patient.

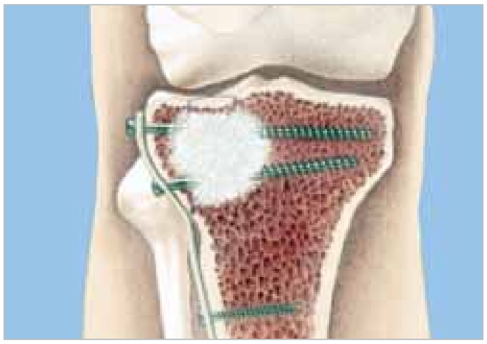


Figure 4. Final construct of combined osteosynthesis and Callos.

CALLOS Impact® Timing Chart

Setting Times		Drilling Times	
Outside Body		**Inside Body**	
Mixing →	1 Minute	Additional Set Time →	2 Minutes
Transfer →	2 Minutes	Ready to Drill → Yes (Callos has been in patient total of 6 mins. already	
Inside Body		Final Tighten? →	Wait 5 Minutes
Implant & Manipulate →	1 Minute	Let Callos set for 5 minutes before doing a final tighten	
Setting (Do not disturb) →	3 Minutes	Final Tighten →	Yes
Total	4 Minutes		
Status → Close - If Drilling Continue →			

CALLOS Inject® Timing Chart

Setting Times		Drilling Times	
Outside Body		**Inside Body**	
Mixing →	1 Minute	Additional Set Time →	4 Minutes
Transfer →	5 Minutes	Ready to Drill → Yes (Callos has been in patient total of 10 mins. already	
Inside Body		Final Tighten? →	Wait 5 Minutes
Implant & Manipulate →	2 Minutes	Let Callos set for 5 minutes before doing a final tighten	
Setting (Do not disturb) →	4 Minutes	Final Tighten →	Yes
Total	6 Minutes		
Status → Close - If Drilling Continue →			

Inject

CALLOS 3 cc Inject Sterile	65-0003-S
CALLOS 5 cc Inject Sterile	65-0005-S
CALLOS 10 cc Inject Sterile	65-0010-S

Impact

CALLOS 5 cc Impact Sterile	65-0105-S
CALLOS 10 cc Impact Sterile	65-0110-S

Callos® can be used in conjuction with the following Acumed Products:

Acu-Loc®
Locking Calcaneal Plates
Polarus® PHP plate

Please contact your local Acumed® Sales Representative to order Callos® for a case.

References

1. Fulmer MT, Ison IC, Hankermayer CR, Constantz BR, Ross J. Measurments of the solubilities and dissolution rates of several hydroxyapatites. Biomaterials. 2002 Feb;23(3):751-5.

2. Hankermeyer CR, Ohashi KL, Delaney DC, Ross J, Constantz BR. Dissolution rates of carbonated hydroxyapatite in hydrochloric acid. Biomaterials. 2002 Feb;23(3):743-50.

3. Smith RA, Long M, Calhoun DN, Fan Z, Rho JY, Cooper M, Margerrison E, Hasty KA, Evaluations of calcium sulfate bone void filler used with a CMC-based hydrogel in an experimental rabbit model, 49th Annual Meeting of the Orthopaedic Research Society, February 2-5, New Orleans, LA, paper #0184.

4. Contantz BR, Ison IC, Fulmer MT, Poser RD, Smith ST, VanWagoner M, Ross J, Goldstein SA, Jupiter JB, Rosenthal DI. Skeletal repair by in situ formation of the mineral phase of bone. Science. 1995 Mar 24;267(5205):1796-9.

5. Frankenburg EP, Goldstein SA, Bauer TW, Harris SA, Poser RD. Biomechanical and histological evaluation of a calcium phosphate cement. J Bone Joint Surg Am. 1998 Aug:80(8):1112-24.

6. Goodman SB, Bauer TW, Carter D, Casteleyn PP, Kyle RF, Larsson S, Sankewich CJ, Swiontkowski MF, Tencer AF, Yetkinler DN, Poser RD. Norian SRS cement augmentation in hip fracture treamtent. Laboratory and intial clinical results. Clin Orthop. 1998 Mar;(348):42-50. Review.

7. Larrson S, Bauer TW. Use of injectable calcium phosphate cement for fracture fixation: a review. Clin Orthop. 2002 Feb;(395):23-32. Review.

8. Sanchez-Sotelo J, Munuera L, Madero R. Treatment of fractures of the distal radius with a remodellable bone cement: a prospective, randomised study using Norian SRS. J Bone Joint Surg Br. 2000 Aug;82(6):856-63.

9. Schildhauer TA, Bauer TW, Josten C, Muhr G. Open reduction and augmentation of internal fixation with an injectable skeletal cement for the treatment of complex calcaneal fractures. J Orthop Trauma. 2000 Jun-Jul;14(5):309-17.

10. Carter, D.R. and Hayes, W.C.: Bone compressive strength: The influence of density and strain rate. Science, 194; 1174-1176, 1976.

11. In Vitro and In Vivo Evaluation of Two Calcium Phosphate Cements Yetkinler, D N; Delaney, D; Constantz, B R Orthopaedic Research Society Transactions Vol.29, San Francisco, California, 2004

12. Surber, B. Establishment of in vitro degradation methods and characterisation of ceramic bone cements. Swiss Society of Biomaterials, Annual Meeting, June 8-9 2000. http://www.aofoundation.org/

13. Cassidy C, Jupiter JB, Cohen M, Delli-Santi M, Fennell C,Leinberry C, Husband J, Ladd A, Seitz WR, Constanz B. Norian SRS cement compared with conventional fixation in distal radial fractures. A randomized study.J Bone Joint Surg Am. 2003 Nov;85-A(11):2127-37

14. Lobenhoffer P, Gerich T, Witte F, Tscherne H. Use of an injectable calcium phosphate bone cement in the treatment of tibial plateau fractures: a prospective study of twenty-six cases with twenty-month mean follow-up. J Orthop Trauma. 2002 Mar;16(3):143-9

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