David S. Warner, M.D., Editor

Vascular Access in Resuscitation

Is There a Role for the Intraosseous Route?

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ABSTRACT

Intraosseous vascular access is a time-tested procedure which has been incorporated into the 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation. Intravenous access is often difficult to achieve in shock patients, and central line placement can be time consuming. Intraosseous vascular access, however, can be achieved quickly with minimal disruption of chest compressions. Newer insertion devices are easy to use, making the intraosseous route an attractive alternative for venous access during a resuscitation event. It is critical that anesthesiologists, who are often at the forefront of patient resuscitation, understand how to properly use this potentially life-saving procedure. **(ANESTHESIOLOGY 2014; 120:1015-31)**

ESTABLISHING vascular access is a critical component of resuscitation during a cardiac arrest. The 2010 American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care emphasize drug administration during cardiac arrest is of secondary importance to high-quality CPR and that interruptions in CPR should be minimized while obtaining intravenous access.[1] Interruptions in CPR decrease coronary perfusion pressure which requires a "rebuilding" period when chest compressions are resumed.[2] Vascular access, however, is still a critical component of resuscitation. A randomized, double-blinded study examining prehospital ventricular fibrillation (VF) demonstrated decreased survival rates from arrest to hospital admission when amiodarone administration was delayed.[3] In addition, a swine model has shown that the time from arrest to drug administration is an independent predictor of return of spontaneous circulation.[4] Given these data, it is clear that the benefits of early vascular access must be considered in conjunction with the importance of uninterrupted CPR. Intraosseous access can be obtained quickly with minimal or no disruption of CPR. As a result, the AHA has proposed providers establish intraosseous access if an intravenous line is not easily obtainable.[1] Similarly, the International Liaison Committee on Resuscitation, as well as the European Resuscitation Counsel, both advocate intraosseous over central venous or endotracheal drug administration if intravenous access cannot be achieved quickly in an emergency.[5] This review aims to examine the literature regarding intraosseous vascular access in the setting of resuscitation, as well as to provide a framework for incorporating the technique into the practice of clinical anesthesia.

Materials and Methods

To answer the question posed, a systematic review was conducted using the PubMed and Ovid Medline databases through August 1, 2013. The primary aim was to determine whether there is a role for intraosseous vascular access in the resuscitation of critically ill patients. Secondary aims were to investigate the evidence regarding clinical use, drug administration, and complications of intraosseous access. The key MeSH terms included: "Infusions, Intraosseous"; "Anesthesiology"; "Critical Care"; "Tibia"; "Advanced Cardiac Life Support"; "American Heart Association"; "Cardiopulmonary Resuscitation"; "Emergency Medical Services"; "Resuscitation/Methods"; "Infusions, Intravenous"; "Catheterization, Central Venous"; "Femoral Vein"; "Sternum"; "Out-of-Hospital Cardiac Arrest"; "Blood Transfusion, Autologous"; "Colloids"; "Hetastarch/Administration and Dosage"; "Bone Marrow/Blood supply"; "Compartment Syndromes"; and "Embolism, Fat." The search was expanded by assessing the reference lists for all retrieved literature. Individual studies were assessed for risk of bias or commercial influence. Only English-language full-text articles published in peer-reviewed journals were

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Table 1. Levels of Evidence

Level	Type of Evidence	Grade of Recommendation
I	Large randomized trials with clear results	A
II	Small randomized trials with uncertain results	B
III	Nonrandomized cohort/case controls	C
IV	Nonrandomized historical controls	C
V	Case series (no controls)	C

Levels of evidence assigned to studies as adapted, with permission, from Sackett. Chest 1989; 95(2 suppl):2S–4.[6] Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

considered. The following inclusion criteria were applied to all studies involved in the clinical use analysis: (1) prospective studies (level of evidence III or higher); (2) focus on insertion success and/or insertion speed; and (3) reporting of complications. Studies were assigned a level of evidence based on Sackett criteria (table 1).[6] One study was excluded over concerns for commercial bias (investigators received free needles and included a manufacturer in the acknowledgments).[7] Another study was excluded as the authors had previously published the same data (original study was used).[8] On the basis of these criteria, a total of 18 studies were included.

History

The principles of intraosseous access were first popularized in 1922 by Cecil K. Drinker, M.D. (1887–1956; Professor, Department of Physiology, Harvard Medical School, Boston, Massachusetts), an anatomist who studied hematopoiesis. He postulated that the capillaries of the marrow cavity could be used as an entry point to systemic circulation.[9] This idea was revisited in the 1940s by Leandro M. Tocantins, M.D. (1901–1963; Professor, Department of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania), who conducted a series of experiments on rabbits for examining intraosseous infusions. He first modeled a hemorrhagic state by aspirating blood from rabbits. The next day, fresh blood was transfused *via* an intraosseous line. Six of seven rabbits had a return to baseline hemoglobin level (one died from complications of the original phlebotomy).[10] Next, he corrected insulin-induced hypoglycemic seizures in rabbits with intraosseous dextrose infusions.[10] In addition, he demonstrated that Congo Red dye injected into the marrow cavity of the tibia reached the heart within 10 s.[10] Tocantins also reported a case series of successful intraosseous infusions of blood and saline in nine pediatric patients with "impossible" intravenous access.[11]

The field of anesthesiology first crossed paths with the concept of intraosseous infusions thanks to the work by Emanuel Papper, M.D., Ph.D. (1915–2002; Professor, Department of Anesthesiology, Columbia-Presbyterian Medical Center, New York, New York). In a study published in Anesthesiology in 1942, he demonstrated that the circulation time for fluids administered *via* intravenous and sternal intraosseous routes was nearly identical.[12] In a series of seven patients, Papper injected 2% sodium cyanide *via* the antecubital vein as well as the sternal intraosseous route and measured the cyanide circulation time to the throat, abdomen, and perineum. Sternal intraosseous injections had an average time to endpoint of 11.4 s, whereas venous injections had an average time of 15.5 s.[12] Papper[12] also described the administration of sodium pentothal in a surgical patient and concluded that it is "possible to administer anesthetic drugs ordinarily given by vein into the sternal marrow with the production of anesthesia in therapeutic doses and toxic manifestations in overdose."

World War II provided an opportunity for wide-spread application of the intraosseous technique. Hamilton Bailey, F.R.C.S., F.A.C.S. (1894–1961; Emeritus Surgeon, Royal Northern Hospital, London, United Kingdom), noted that the sternal intraosseous route could be effectively used even in black-out conditions.[13] He developed a special trocar to prevent the needle from penetrating the back wall of the sternum and injuring the heart. As a result, sternal intraosseous needles were included in emergency medical supply kits during World War II.[14] As military medical personal returned home after the war, the practice of intraosseous infusion was largely forgotten. This can be explained by both the development of better plastic intravenous catheters and the absence of formal paramedics groups. The concept of intraosseous access was "re-discovered" in the early 1980s by James P. Orlowski, M.D. (Department of Pediatrics, Cleveland Clinic Foundation, Cleveland, Ohio). Orlowski, a pediatrician, visited India during a cholera epidemic and observed intraosseous infusions saving the lives of severely dehydrated children. He subsequently published an editorial entitled "My kingdom for an intravenous line" which helped lead to the incorporation of intraosseous access into Pediatric Advanced Life Support.[15]

Anatomy and Physiology

Peripheral veins can collapse in a state of hemorrhage or dehydration. The intraosseous space, however, is a noncollapsible entry point into the systemic circulation. A vast central sinus, composed of distensible endothelium, runs in the middle of the diaphysis. This sinus can distend to accommodate a fivefold increase in volume.[16] Blood vessels of the intraosseous space are connected to the systemic circulation by a series of longitudinal Haversian canals containing a small artery and vein. The Haversian canals are linked to a system of Volkmann canals which penetrate the cortex and terminate in connections with the osseous venous drainage. The proximal tibia, a common site of intraosseous insertion, ultimately drains to the popliteal vein. The distal tibia drains to the saphenous vein, whereas the proximal humerus connects with the axillary vein.

The mean blood pressure in the medullary space is approximately 20 to 30 mmHg, or approximately one third of systemic mean pressure.[17] Therefore, fluid administration often requires a pressure bag to achieve optimal flow rates. *Depending on the infusion characteristics and clinical*

scenario, it will likely be necessary to augment the infusion rates of intraosseous lines with a pressure bag or rapid infusion device. Flow rates can also be influenced by hypoxia, hypercarbia, and acidosis (often present during resuscitation) leading to local vasodilation and increased intraosseous blood flow.

Opportunities of the Intraosseous Route, Insertion, and Devices

Insertion Speed

The 2010 AHA guidelines state that "*it is reasonable for providers to establish intraosseous access if intravenous access is not readily available.*"[1] This recommendation is in part due to several studies[18–22] demonstrating that intraosseous access can be achieved quickly and effectively in a variety of clinical settings. One trial examining 60 dehydrated children (aged from 3 months to 2 yr) found a 5-min success rate of 100% for intraosseous insertion *versus* just 67% success for peripheral intravenous catheter placement.[18] A prospective study of adult patients (medical and trauma patients in the emergency department setting) compared intraosseous cannulation with central venous access in patients with "impossible" intravenous access. Intraosseous access was achieved on the first attempt 90% of the time *versus* just a 60% first-attempt success rate for central line placement.[19] In addition, intraosseous cannulation took significantly less time than central line placement (intraosseous: 2.3 ± 0.8 min *vs.* central line: 9.9 ± 3.7 min; $P < 0.001$).[19] A prospective simulation study examining intraosseous insertion in the prehospital setting found that access could be established in less than 1 min 84.8% of the time, even in an ambulance traveling 35 mph speed with sudden starting and stopping.[20]

Establishing peripheral venous access in a prehospital setting can be challenging. Prehospital success rates vary from 43 to 91%.[18,21,23,24] A retrospective chart review of 641 adult patients with attempted intravenous catheter placement in a moving ambulance found a success rate of just 80%.[23] Intraosseous cannulation has been shown to be rapid and effective specifically in the setting of prehospital cardiac arrest. In a randomized trial of 182 patients receiving vascular access for nontraumatic cardiac arrest, tibial intraosseous access was achieved on the first attempt 91% of the time as compared with just a 43% first-attempt success rate for peripheral venous access.[21] In another trial, emergency medicine residents treating cardiac arrest in a high-fidelity simulator placed intraosseous lines significantly faster than central lines (intraosseous: 49.0 s *vs.* central: 194.6 s).[22] When considered collectively, these studies indicate that intraosseous access can be achieved faster and with fewer attempts in critical situations.

Obtaining access quickly in cardiac arrest can have a substantial impact on outcome. In a prospective study, 30 swine in VF were randomized to receive epinephrine (intravenous or intraosseous) or placebo.[25] To simulate realistic scenarios of successful vascular access, intraosseous epinephrine was administered 1 min after onset of CPR, whereas intravenous epinephrine was administered after an 8-min delay. At equivalent doses, early intraosseous epinephrine administration resulted in a shorter time to return of spontaneous circulation, decreased total defibrillation energy, and better 24-h survival than delayed intravenous epinephrine.[25] These results are consistent with another swine model of VF which concluded that early intraosseous epinephrine resulted in decreased time to return of spontaneous circulation, faster termination of VF, and better 20-min survival.[26]

Historically, resuscitation drugs have been administered *via* an endotracheal tube in instances where intravenous access cannot be obtained. However, resuscitation drugs administered *via* the trachea have lower peak plasma concentrations compared with the peak plasma concentrations of the same drugs given intravenously.[27] Therefore, the 2010 AHA guidelines stipulate that endotracheal administration of resuscitation drugs should only be considered if attempts at both intravenous and intraosseous access have failed.[1]

Infection Risk

It is difficult to directly compare the infectious risk of central venous catheters and intraosseous lines placed during a resuscitation event as there are no head-to-head studies in this setting. In most instances, central lines are left in place for extended periods of time, whereas intraosseous lines generally serve as a short-term means of vascular access. The infection risks of these routes independently have been described. A recent meta-analysis of central venous catheters found no significant difference in the risk of catheter-related bloodstream infections between the femoral and internal jugular sites (risk ratio, 1.35; 95% CI, 0.84–2.19; $P = 0.2$; $I = 0\%$).[28] Despite these findings, the 2013 Joint Commission National Patient Safety Goals state that providers should "*NOT insert catheters into the femoral veins unless other sites are unavailable.*"* Central venous access during code situations is often obtained with suboptimal sterile technique and without the use of proper barrier precautions. In a retrospective review of adult trauma patients (emergency department, operating room, and intensive care settings), 25 of 35 (71%) diagnosed central line–associated blood stream infections occurred in patients with known breaches in sterile technique.[29]

The use of intraosseous access in an emergency setting allows clinicians to avoid placing femoral lines and obviates the potential for improper barrier precautions and less than ideal sterile technique. A meta-analysis examining 30 studies and 4,270 patients concluded that there was a 0.6% incidence rate of osteomyelitis attributed to intraosseous cannulation.[30] Most infections occurred during prolonged infusions or in situations of concurrent bacteremia at the time of insertion.[30] This dated meta-analysis was conducted before the advent of insertion-assist devices and looked only at manual needle insertion.

* The Joint Commission: National Patient Safety Goals effective January 1, 2013. Available at: http://www.jointcommission.org/assets/1/18/NPSG_Chapter_Jan2013_HAP.pdf. Accessed May 1, 2013.

A more recent prospective, randomized trial involving the EZ-IO® (Vidacare Corporation, San Antonio, TX) and Bone Injection Gun (BIG®; Waismed, Houston, TX) intraosseous insertion devices in adult patients was conducted in an emergency department resuscitation setting. In this study, zero infections were reported in 40 patients receiving intraosseous lines with one of the two devices.[31] Similarly, two prospective studies of 60 (adult) and 30 (25 adult and 5 pediatric cardiac arrest patients) intraosseous insertions using the EZ-IO® device, both reported no cases of infection.[32,33] Larger studies, including direct comparisons of central and intraosseous lines placed during resuscitation, represent an area of future research.

Drug Delivery

Intraosseous access is equivalent to intravenous access in terms of functionality and drug delivery. This was demonstrated by Papper[12] in 1942 and has subsequently been verified in other studies. Orlowski used a canine model to examine peak effect and serum concentrations of commonly used emergency drugs. He demonstrated equivalency of the intraosseous route to peripheral and central venous drug administration for epinephrine, sodium bicarbonate, calcium chloride, hydroxyethyl starch, and normal saline.[34] A prospective, randomized, crossover pharmacokinetic study was conducted to compare the bioequivalence of morphine administered by intraosseous and intravenous routes in adult patients with cancer (nonresuscitation setting). Each patient had both an intravenous and intraosseous line and was randomized to receive 5 mg of morphine *via* one route, followed by 5 mg of morphine by the other route 24 h later. No statistically significant differences were observed between the intravenous and intraosseous routes in calculated pharmacokinetic data including peak concentration and time to peak concentration.[35] Another study used a swine model of VF to demonstrate intraosseous epinephrine administered during CPR is rapidly transported to the central circulation and results in a dose-dependent increase in mean arterial blood pressure.[36] More recently, the pharmacokinetics of intraosseous drug delivery has been compared with central venous drug delivery. A "double dye tracer technique" was used in a swine cardiac arrest model to compare simultaneous epinephrine injections in the sternum and tibia. Peak plasma concentrations were achieved faster with the sternal route than the tibia route (sternal: 53 ± 11 s *vs.* tibia: 107 ± 27 s; $P = 0.03$).[37] The time to peak blood concentration was similar for both routes (sternal: 97 ± 17 s *vs.* central: 70 ± 12 s; $P = 0.17$).[37] The authors concluded that intraosseous administration of medications through both the sternum and tibia are effective during CPR in anesthetized swine, but the sternal route results in faster uptake.[37] As per the 2010 AHA guidelines, all Advanced Cardiac Life Support medications are administered at the same doses regardless of route.[1] A summary of available clinical data showing intraosseous medication dosing in adult and pediatric patients is presented in table 2.[1,11,30,34,35,38–59]

Volume Resuscitation

Both the intraosseous and intravenous routes also offer equivalent delivery of resuscitative fluid. The safety and efficacy of intraosseous packed erythrocyte transfusion are well documented. A prospective study (swine model) demonstrated that radiolabeled erythrocytes administered *via* the intraosseous route were rapidly delivered to systemic circulation (30 s to 1 min).[60] The safety of intraosseous blood transfusion was shown in a randomized, controlled, blinded swine study. Phlebotomized animals received a transfusion by either an intravenous catheter or an intraosseous line. In both groups, blood pressure returned to baseline values within 15 min, and laboratory studies assessing for disseminated intravascular coagulation were negative.[61] In addition, there was no evidence of fat embolism or inflammation on pathologic examination of the lungs or kidneys in the intraosseous group.[61] Crystalloids and colloids have also been effectively administered through the intraosseous route. An analysis of hydroxyethyl starch pharmacokinetics demonstrated no significant difference between intravenous and intraosseous administration in hypovolemic swine.[62] Crystalloid infusion *via* the intraosseous route has been demonstrated to be as effective as the central or peripheral route in treating hemorrhagic shock in a swine model.[63]

Diagnostic Studies

The intraosseous medullary space can also serve as a source of blood for laboratory analysis. The initial aspirate after intraosseous line placement can be used for routine laboratory tests after wasting 2 ml of the marrow/blood mixture.[64] In a study involving human volunteers, blood samples were drawn simultaneously from both a peripheral vein and the intraosseous space. Analysis revealed a significant correlation between venous and intraosseous samples for hemoglobin, hematocrit, glucose, blood urea nitrogen, and creatinine. Carbon dioxide and platelet measurements may be lower in intraosseous samples, whereas the leukocyte count may be higher.[64] Blood gas measurements from intraosseous blood are "intermediate" between arterial and venous blood gases, suggesting intraosseous samples correspond with arterialized capillary blood samples.[65] Intraosseous blood samples can also be used to obtain a reliable type and cross. A prospective study comparing simultaneous intraosseous and venous blood draws in humans found no difference in the accuracy of ABO and Rh typing.[66] Laboratory values from an intraosseous line may not be accurate after a sustained infusion.[52] Given these data, it is evident that blood samples drawn immediately after intraosseous cannulation can provide accurate laboratory and blood bank data to aid in resuscitation.

Cost Effectiveness

A multicenter, observational study compared the costs of central venous catheter insertion with the cost of intraosseous insertion in unstable patients presenting to the emergency department. A total of 105 patients received intraosseous access (85% were "medical" patients and 53%

Table 2. Resuscitative Medications and Fluids *via* the Intraosseous Route

Therapy	Maximum Reported Intraosseous Dose	Adult (A)/ Pediatric (P)	Comments/Limitations
Medications			
Adenosine[38–40]	0.05–0.25 mg/kg	P	Mixed effectiveness in case reports
Amiodarone[1,41]	300 mg	A	ACLS: same dose intraosseous/intravenous
Atropine[1,42–44]	A: 3 mg (total) P: 5 μg/kg	A/P	Division/interval of doses not specified ACLS: same dose intraosseous/intravenous
Bretylium[44]	Not specified	A/P	Prehospital use reported
Calcium chloride[34,44–47]	Not specified	A/P	"Safe use" reported without details
Cisatracurium[46]	Not specified	Not specified	"Safe use" reported without details
Dextrose (10–50%)[34,38,44,48–50]	Not specified	A/P	Reports of soft-tissue injury with extravasation of hypertonic solutions
Dobutamine[48,53,54]	10 μg kg^{-1} min^{-1}	P	Physiologic response in 6 month old
Dopamine[38,48,53,54]	P: 10 μg kg^{-1} min^{-1}	A/P	Adult dose not reported
Epinephrine[1,34,42,44,55]	A: 1 mg A: 0.02 μg kg^{-1} min^{-1} P: 10 μg/kg	A/P	ACLS: same dose intraosseous/intravenous Soft-tissue necrosis reported with extravasation
Etomidate[46]	Not specified	Not specified	"Safe use" reported without details
Fentanyl[42,48]	Not specified	A	"Safe use" reported without details
Heparin[41,51,52]	3,000 U	A/P	Used in acute myocardial infarction
Insulin[45,51]	Not specified	A/P	"Safe use" reported without details
Lidocaine[30,44,48]	Not specified	A/P	"Safe use" reported without details
Morphine[35,45,47]	Not specified	A/P	"Safe use" reported without details
Naloxone[38,44,48]	Not specified	A/P	"Safe use" reported without details
Norepinephrine[48,55]	Not specified	A	Soft-tissue necrosis reported with extravasation
Phenytoin[38,45,47,48,56]	17 mg/kg	P	Potentially delayed peak plasma levels
Propofol[43]	P: 2 mg/kg	A/P	Used in 8-month-old patient weighing 5.4 kg
Rocuronium[48]	Not specified	A	Multiple reports of unspecified "muscle relaxants"
Sodium bicarbonate[34,44,45,55]	Not specified	A/P	Tissue necrosis reported with extravasation
Succinylcholine[38,45,47,48]	Not specified	A/P	Multiple reports of unspecified "muscle relaxants" and rapid sequence inductions
Tenecteplase[41,42]	7,000 U	A	Successful fibrinolytic therapy (myocardial ischemia and pulmonary embolism)
Vasopressin[1,48]	40 units	A	ACLS: same dose intraosseous/intravenous
Vecuronium[42,45,47,48]	0.1 mg/kg	A/P	Multiple reports of unspecified "muscle relaxants"
Resuscitative fluid			
Albumin[50]	26–42 ml/kg	P	Used in 41-day-old patient weighing 1,950 g
Fresh-frozen plasma[30,51]	Not specified	A/P	"Safe use" reported without details
Hypertonic saline[58,59]	Not specified	A	Tissue necrosis reported with extravasation
Lactated Ringer's solution[44,53,56]	P: 60 ml/kg	A/P	Pediatric dosing in burn patients
Normal saline[11,38,42,51,53]	Not specified	A/P	Multiple reports of "safe" infusion
Packed erythrocytes[11,38,47,57]	P: 10 ml/kg	A/P	Case reports ages 5 months and older

A summary of commonly used resuscitation medications administered *via* the intraosseous route in humans. Where possible, reported dosing, patient population (adult *vs.* pediatric), and limitations have been specified.

ACLS = advanced cardiac life support.

presented with cardiac or respiratory arrest), and costs were compared with published central line data. Cost savings of intraosseous placement over of central venous access were found to be $195 per procedure.[67] However, this study has limitations that must be considered. It focused only on initial insertion costs in the emergency department and did not address issues such as daily central line maintenance costs or the percentage of patients in the intraosseous group who eventually received central lines during their hospital admission. The percentage of patients who later require central access has not been studied and must be determined before true conclusions of "overall" cost effectiveness can be made.

Insertion Sites

Early pioneers of intraosseous access tended to focus on the sternum as the preferred insertion site. The sternum offers easy accessibility and close proximity to the central venous circulation *via* the mammary veins. Time to peak blood concentration of epinephrine injected through a sternal intraosseous needle is similar to epinephrine injected through a central line (intraosseous: 97 ± 17 s *vs.* central: 70 ± 12 s) in a swine model of cardiac arrest.[37] In the same study, the sternal intraosseous site achieved peak arterial epinephrine concentrations significantly faster than the tibial intraosseous site (sternum: 53 ± 11 s *vs.* tibial: 107 ± 27 s; $P = 0.3$).[37] There

are, however, several disadvantages of the sternal site. Chest compressions must be briefly interrupted during insertion. It also carries the risk of inadvertently puncturing the heart or great vessels. Pediatric patients are more susceptible to injury from sternal intraosseous insertion due to the proximity to the great vessels and the small size of the marrow cavity (with subsequent poor flow). As a result, the FAST1® (Pyng Medical Corporation, Richmond, British Columbia, Canada) sternal insertion device is not approved for patients less than 12 yr of age.

Although the sternal site is of important historical significance, most providers favor the proximal tibial site. In a survey of emergency-room physicians, 84% selected the proximal tibia as their preferred insertion site. Just 10% of physicians surveyed preferred the humerus and another 10% chose the medial malleolus.[68] Although the sample size of this survey was small, it is consistent with newer intraosseous studies supporting the proximal tibia as a safe, easily accessible site. A prospective study of 182 patients compared proximal tibia and humeral intraosseous insertion sites head-to-head. The proximal tibia group had a higher first-attempt success rate (tibia: 91% *vs.* humerus: 51%) and faster insertion time (tibia: 4.6 min *vs.* humerus: 7.0 min) than the humeral group.[21] In newborns, the needle should be inserted 10-mm distal to the anterior tibial tuberosity and aimed in a slight posterior and inferior direction to avoid damaging the growth plate.[69] In children and adults, the needle insertion site is 2 cm below the tibial tuberosity and 1 cm medially on the tibial plateau (fig. 1) (see video, Supplemental Digital Content 1, http://links.lww.com/ALN/B32, which is a guide to intraosseous insertion).[48]

For adults or skeletally mature adolescents, the proximal humerus is another potential intraosseous site. The patient is positioned with their arm adducted and internally rotated (placing the patient's hand on their abdomen facilitates proper positioning). The acromion process is then palpated and the greater tubercle of the humerus is located 2 cm distal to this point (fig. 2) (see video, Supplemental Digital Content 1, http://links.lww.com/ALN/B32, which is a guide to intraosseous insertion). The humeral site has a lower first-attempt success rate compared with the tibia and it has a higher rate of needle dislodgement.[21] This can delay medication administration during cardiac arrest and may lead to more complications from fluid extravasation.[21]

Although there are practical disadvantages such as needle dislodgement with the humeral intraosseous site, it may offer the benefit of higher flow rates. Flow rates of fluid through EZ-IO® needles placed in the humerus, tibia, and femur of swine were compared in a prospective interventional study. The humerus had a statistically significant ($P < 0.001$) higher flow rate (213 ml/min) compared with that of the tibia (103 ml/min) or femur (138 ml/min) when saline was infused *via* a pressure bag.[70] Human studies comparing flow rates of the humerus and tibia offer mixed results. A study of 10 human volunteers demonstrated a significantly higher mean flow rate at the humeral site (humerus: 5,093 ± 2,632 ml/h *vs.* tibia 1,048 ± 831 ml/h) with a pressurized infusion.[71] However, a prospective observational study of 24 critically ill patients (emergency department setting) comparing humeral and tibial EZ-IO® flow

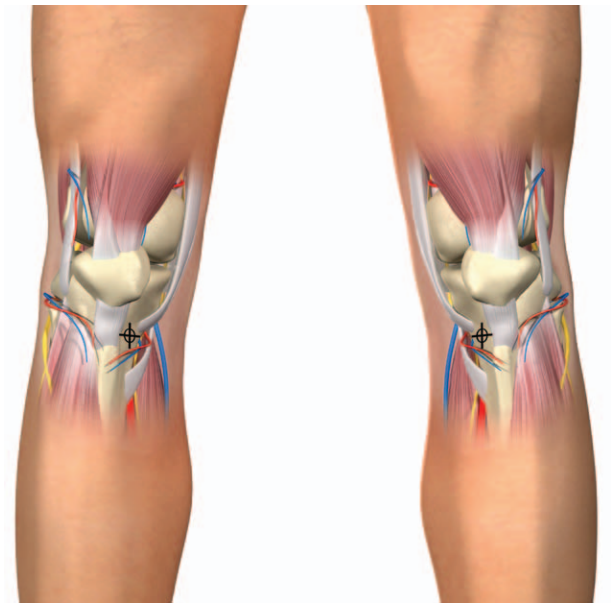

Fig. 1. Identification of proximal tibia insertion site. Reproduced, with permission, from Vidacare Corporation, San Antonio, Texas.

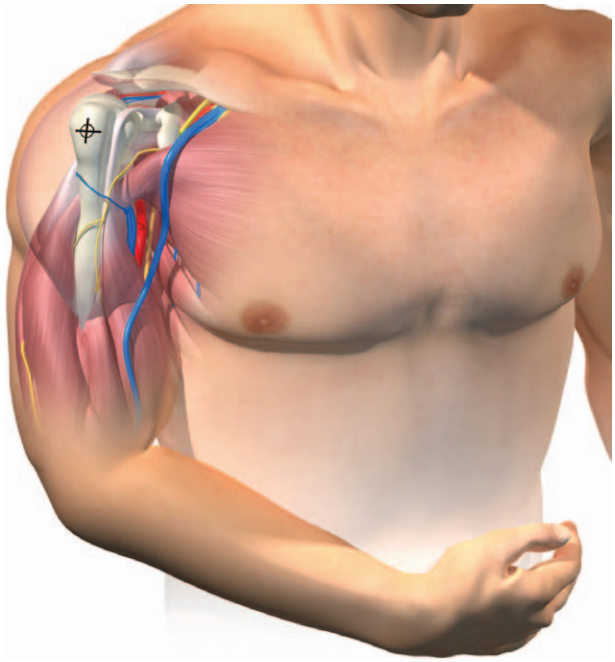

Fig. 2. Identification of proximal humerus insertion site 2 cm distal to the acromion process. Reproduced, with permission, from Vidacare Corporation, San Antonio, Texas.

rates demonstrated no statistically significant difference between sites (humerus: 153 ml/min *vs.* tibia: 165 ml/min). Both sites in this study had significantly faster flow rates with a pressurized infusion bag than with gravity drip.[72] On the basis of these small swine and human studies, the humeral site may offer higher flow rates than the tibia, but trials with larger sample sizes are needed to make a conclusive determination. For comparison, a prospective study of human volunteers showed a mean infusion rate of 35.6 ml/min *via* an 18-gauge intravenous catheter (gravity drip).[73] Higher intravenous flow rates (18 gauge: 205 ml/min; 16 gauge: 412 ml/min) have been demonstrated using a Rapid Infusion System (Haemonetics Corp., Braintree, MA).[74]

Insertion Devices

Manual Needles. Manually inserted intraosseous needles have evolved significantly since the early experiments in the 1920s. Several manufacturers now produce inexpensive needles with specialized handles specifically designed for intraosseous use (fig. 3). Insertion techniques are similar for all of the manual needle types. The needle is oriented perpendicular to the entry site and pressure is applied in conjunction with a twisting motion until a "loss of resistance" is felt as the needle enters the marrow cavity (see video, Supplemental Digital Content 1, http://links.lww.com/ALN/B32, which is a guide to intraosseous insertion).

The Near Needle Holder (Near Manufacturing, Camrose, Alberta, Canada) is a reusable handle device which allows a standard hollow needle to be inserted in the intraosseous space (fig. 4). A group of physicians and medical students in Guyana attempted simulated insertion of both needle types after watching a short training video. Insertion times for both types were nearly identical (Near Needle Holder: 32 ± 13.2 s *vs.* Cook: 32 ± 12.3 s), and most users rated the Near Needle Holder as safe and easy to use.[75] The Near Needle Holder may potentially be a safe, inexpensive option in developing countries (it is not approved for use in the United States) or areas with limited resources.

Fig. 3. Cook® (Cook Critical Care, Bloomington, IN) disposable intraosseous needle.

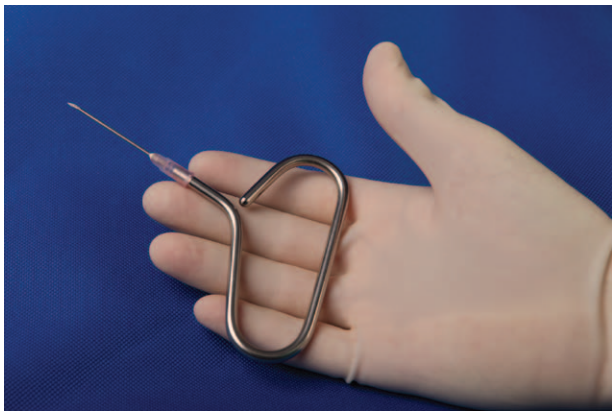

Fig. 4. The Near Needle Holder (Near Manufacturing, Camrose, Alberta, Canada) with 16-gauge angiocatheter.

Fig. 5. The FAST1® sternal intraosseous insertion device. Reproduced, with permission, from Pyng Medical Corporation, Richmond, British Columbia, Canada.

Reported first-attempt success rates with manual needles range widely. One study demonstrated an overall success rate of 67.7% with four needle types (standard hypodermic, bone marrow needle, spinal needle, and manual intraosseous needle) inserted by resident physicians in anesthetized piglets.[76] In another simulation study, medical students had a 95% success rate inserting a SurFast® (Cook Critical Care, Bloomington, IN) needle in animal bones.[77] Success rates as high as 85% have been reported in pediatric patients (less than 5 yr old) presenting in prehospital cardiac arrest.[77,78] More recently, prehospital first-attempt success rates were found to be 78% using a variety of intraosseous needles.[45]

Impact-driven Devices.

FAST1®. The FAST1® is a single-use device designed for placement in the manubrium (fig. 5). Insertion is aided by user-applied force. A stick-on target placed at the sternal notch guides proper placement. The device has 10 stabilizing needles (which do not enter the bone), which are used to prevent overpenetration through the sternum. Reported infusion rates are 30 to 80 ml/min by gravity drip, 120 ml/min by pressurized source, and 250 ml/min by syringe injection.† The FAST1® device may be of particular value in cases of traumatic amputation of the extremities.

The FAST1® device seems to have a quick learning curve. A pilot study of success rates found that first-time users of

† Pyng Medical Corporation: FAST1® specifications. Available at: http://www.pyng.com/wp/wp-content/uploads/2011/04/PM-130a%20FAST1%20Spec%20Sheet-compressed.pdf. Accessed May 10, 2013.

Table 3. Review of Recent FAST1® (Pyng Medical Corporation, Richmond, British Columbia, Canada) Clinical Trials

Publication and Level of Evidence	Study Design	Setting and Endpoints	Age (Mean)	Pediatric, n (%)	Insertions, n
Macnab[79] Level III	Prospective, observational	Prehospital success/time	Not reported	Not reported	FAST1®: 50
Frascone[82] Level III	Prospective, observational	Prehospital success rate	55.1	0	FAST1®: 89
Calkins[81] Level III	Prospective, observational	Simulation insertion success/ time	Cadaver insertion	Not reported	FAST1®: 30
Byars[83] Level III	Prospective, observational	Prehospital insertion success	Not reported	Not reported	FAST1®: 41
Overall	—	—	55.1	0	210

A summary of recent clinical trials examining FAST1® use. Cadaver data from Calkins *et al.*[81] were excluded from overall calculations of cardiac arrest, trauma, and complications.
N/A = not applicable.

Fig. 6. Pediatric BIG® intraosseous insertion device with adjustable needle length. Reproduced, with permission, from Waismed, Houston, Texas.

FAST1® had a 74% rate of success.[79] After just one experience using the device, the success rate increased to 95% on subsequent attempts with the median insertion time for all subjects being 60 s (prehospital and emergency department setting).[79] A simulation study found that after a 2-h lecture, 96.6% of emergency medical technician students properly identified anatomic landmarks and 100% placed the target sticker correctly. Overall, students had a 93.1% rate of successful needle deployment in a mannequin.[80] Given the usage of the FAST1® device in patients with extremity amputations, a study was conducted to examine the training required for military medical personnel to become proficient in its use. After a 60-min lecture, a training video and simulation session, study subjects correctly placed the FAST1® in a cadaver 29 of 30 times (94%) with a mean time of 114 ± 36 s.[81] Some failed attempts at FAST1® in these studies have been attributed to technical difficulties arising from patient obesity.[79] For a summary of recent prospective studies examining FAST1®, see table 3.[79,81–83]

BIG®. The BIG® is a single-use, spring-loaded insertion device which is available in adult (15 gauge) and pediatric (18 gauge) sizes (fig. 6). The device is held perpendicular to the insertion site and the spring released. After deployment, an internal trocar is removed and the safety latch is used to help secure the device in place. Reported

Table 4. Review of Recent BIG® (Waismed, Houston, TX) Clinical Trials

Publication and Level of Evidence	Study Design	Setting and Endpoints	Age (Mean)	Pediatric, n (%)	Insertions (n)
Leidel[31] Level II	Prospective, randomized, controlled	Emergency department success/ time	43	0	BIG®: 20
Calkins[81] Level II	Prospective, randomized, controlled	Cadaver insertion success/time	N/A	Not reported	BIG®: 31
Schwartz[84] Level III	Prospective, observational	Prehospital insertion success	53	47 (25)	BIG®: 189
Gerritse[85] Level III	Prospective, observational	Prehospital insertion success	Not reported	14 (35)	BIG®: 40
Overall	—	—	48	61 (22)	280

A summary of recent prospective clinical trials examining BIG® use. Cadaver data from Calkins *et al.*[81] were excluded from the overall calculation of complications.
N/A = not applicable.

Tibia Insertion, n (%)	Humerus Insertion, n (%)	Cardiac Arrest, n (%)	Trauma, n (%)	Insertion Success, n (%)	Insertion Time (s) (mean)	Complications
N/A	N/A	15 (30)	9 (18)	42 (84)	77	None reported
89 (100)	0	Not reported	Not reported	64 (72)	Not reported	None reported
Not specified	Not specified	N/A	N/A	29 (94)	114	N/A
N/A	N/A	Not specified	Not specified	30 (73)	67	Two minor bleeding at insertion site
89 (42)	0	15 (8)	9 (5)	165/210 (79)	86	2/180 (1%)

first-attempt insertion success rates for the BIG® range from 71 to 91%.[31,84,85] A prehospital study evaluating BIG® use by a helicopter-transport emergency medical team found a 71% overall success rate (adult and pediatric) and reported no complications.[85] In a canine study, success rates for manual needle and BIG® insertion were similar. Insertion of the BIG® device, however, was significantly faster (BIG®: 22.4 ± 8.2 s *vs.* manual: 42.0 ± 28.1 s).[86] The BIG® device is easy to learn and requires minimal training. Military medical personal with no previous experience were successful in 29 of 31 BIG® insertion attempts (in cadavers) after a lecture and training video.[81] For a summary of recent prospective studies examining BIG® use, see table 4.[31,81,84,85]

Battery-powered Devices (EZ-IO®). The EZ-IO® is a lithium-battery–powered driver with three different needle sizes to choose from (fig. 7). The needles are all 15 gauge and differ only in length (15, 25, and 45 mm). A number of studies have been conducted to look at the speed and accuracy of EZ-IO® insertion. A randomized trial compared EZ-IO® insertion with a manual needle technique in adult cadavers. Although insertion times were similar (EZ-IO®: 32 ± 11 s *vs.* manual: 33 ± 28 s), the EZ-IO® had a higher "user friendliness" rating and a better first-attempt success rate (EZ-IO®: 97.8% *vs.* manual: 79.5%).[87] When compared head-to-head with BIG® insertion, the EZ-IO® device has a higher first-attempt success rate (EZ-IO®: 90% *vs.* BIG®: 80%) and faster insertion times (EZ-IO®: 1.8 min *vs.* BIG®: 2.2 min) in the emergency department resuscitation setting (trauma and medical patients).[31] A 7-yr retrospective analysis of prehospital insertion determined that EZ-IO® placement has a significantly higher first-attempt success rate compared with the first-attempt success rate of both manual and BIG® insertion (EZ-IO®: 96% *vs.* manual: 50% *vs.* BIG®: 55%).[88]

The EZ-IO® device is easy to use and requires minimal training. A group of 99 medical providers with no EZ-IO® experience were given a 5-min presentation with one insertion demonstration. They each then performed three tibia insertions on cadavers. Success rates for the three attempts were 96.9, 94.9, and 100%, respectively, with a median time of just 6 s.[89] In another study, paramedic students received a video-based training on EZ-IO® and BIG® devices. Participants had a significantly higher first-attempt success rate (in turkey bones) with the EZ-IO® (EZ-IO®: 28 of 29 *vs.* BIG®: 19 of 29).[90] These studies suggest that the EZ-IO® is an easy to use, easy to learn tool that can be used successfully in resuscitation scenarios with minimal training. For a summary of recent prospective studies examining EZ-IO® use, see table 5.[8,21,31–33,46,67,72,82,91–95]

Tibia Insertion, n (%)	Humerus Insertion, n (%)	Cardiac Arrest, n (%)	Trauma, n (%)	Insertion Success, n (%)	Insertion Time (s) (Mean)	Complications
11 (55)	11 (55)	Not reported	15 (75)	16 (80)	132	Two extravasations from humeral insertion
Not specified	Not specified	N/A	N/A	29 (94)	70	N/A
Not specified	Not specified	71 (74)	34 (18)	172 (91)	Not reported	None reported
Not specified	Not specified	21 (53)	Not reported	Adult: 19 (73) Pediatrics: 10 (71)	Not reported	None reported
11 (4)	11 (4)	92 (33)	49 (18)	217/249 (87%)	101	2/249 (0.8%)

Fig. 7. EZ-IO® needle driver with 15 mm (*pink*), 25 mm (*blue*), and 45 mm (*yellow*) needles. Reproduced, with permission, from Vidacare Corporation, San Antonio, Texas.

Clinical Use

Intraosseous vascular access may be indicated in emergency situations where venous access cannot be obtained quickly. These include trauma, cardiac arrest, status epilepticus, burn, and shock patients.[96] Several prospective human studies have examined intraosseous insertion speed and success rate (with multiple insertion devices) in the prehospital and emergency department setting. In the studies cited in this review, the overall insertion success rate was 90% (1,228 of 1,367) across all devices. Individually, the FAST1®, BIG®, and EZ-IO® devices had insertion success rates of 79, 87, and 90%, respectively (tables 3–5). The mean insertion time was relatively fast for all the three insertion devices (FAST1®: 86 s; BIG®: 101 s; and EZ-IO®: 60 s) (tables 3–5). For a summary guide to clinical use, see figure 8.

Contraindications

There are few absolute contraindications to intraosseous use as the route is primarily used in life-threatening situations. Most absolute contraindications are related to anatomic abnormalities.

Table 5. Review of Recent EZ-IO® (Vidacare Corporation, San Antonio, TX) Clinical Trials

Publication and Level of Evidence	Study Design	Setting and Endpoints	Age (Mean)	Pediatric, n (%)	Insertions (n)
Leidel[31] Level II	Prospective, randomized, controlled	Emergency department success/time	43	0	EZ-IO®: 20
Santos[32] Level III	Prospective, observational	Prehospital success	47	14 (24)	EZ-IO®: 60
Schalk[91] Level III	Prospective, observational	Prehospital success/time	66	5 (6)	EZ-IO®: 77
Tan[92] Level III	Prospective, observational	Emergency department flow rates	Not reported	0	EZ-IO®: 42
Torres[93] Level III	Prospective, observational	Prehospital insertion time	56	0	EZ-IO®: 114
Dolister[67] Level III	Prospective	Emergency department success/time	48	0	EZ-IO®: 105
Gazin[33] Level III	Prospective, observational	Prehospital success rate	57	5 (12)	EZ-IO®: 39
Reades[21] Level III	Prospective, randomized	Prehospital success rate	65	0	EZ-IO®: 115
Reades[94] Level III	Prospective, observational	Prehospital success rate	63	0	EZ-IO®: 88
Ong[72] Level III	Prospective, observational	Emergency department success and flow rates	Not reported	0	EZ-IO®: 35
Paxton[46] Level III	Prospective, observational	Emergency department success rate	46.9	0	EZ-IO®: 29
Horton[95] Level III	Prospective, observational	Emergency department success rate	5.5	95 (100)	EZ-IO®: 95
Frascone[82] Level III	Prospective, observational	Prehospital success rate	55.1	0	EZ-IO®: 89
overall	—	—	50.2	119 (13%)	908

A summary of recent prospective clinical trials examining EZ-IO® use in prehospital and emergency department resuscitation settings.

Absolute Contraindications[79,84,91,97]‡,§

1. Fracture in target bone (risk of fluid extravasation)
2. Compartment syndrome in target extremity
3. Vascular injury in target extremity
4. Acute infection at insertion site
5. Previous orthopedic surgery with hardware at insertions site
6. Recent failed intraosseous attempt in same extremity (within 24–48 h)
7. Inability to identify landmarks
8. History of sternotomy (for FAST1®)
9. Sternal thickness less than 6.5 mm (for FAST1®)

Relative Contraindications[79,84,97–99]

1. Cellulitis or burns of target extremity
2. Osseous abnormalities such as osteogenesis imperfect or severe osteoporosis
3. Right-to-left intracardiac shunts (fat or bone marrow cerebral embolic risk)
4. Sepsis or bacteremia
5. Inferior vena cava injury

‡ Vidacare Corporation: Who needs an IO device? Available at: http://www.vidacare.com/EZ-IO/Clinical-Applications-Who-needs-an-IO-device.aspx. Accessed May 10, 2013.

§ Pyng Medical Corporation: FAST1® Protocol Guide. Available at: http://www.pyng.com/products/fast1/clinical-and-technical-information/protocol/?pi=51. Accessed May 10, 2013.

Complications

A total of 1,367 intraosseous insertions were reported in the studies cited in this review (908 EZ-IO®; 249 BIG®; 210 FAST1®). These insertions were associated with 23 reported complications for an overall complication rate of 1.6%. Of these 23 complications, 12 can be considered "minor" (10 needle dislodgements and 2 reports of minor bleeding at site). Excluding these minor complications, the overall complication rate for studies cited in this review was 0.80% (tables 3–5). A recent retrospective cohort study involving 291 pediatric patients with intraosseous lines placed in a variety of settings found zero associated complications.[100] The most commonly reported complication is extravasation of fluids. Reported extravasation rates vary widely, ranging from 1 to 22%.[101] Risk factors include: incorrect needle placement, multiple punctures in the same bone, and incorrect needle length.[101] Osseous punctures can take 12 to 48 h to clot; therefore, subsequent intraosseous placement in the same bone should be avoided during that period. Inadequate needle length can lead to higher rates of dislodgement and extravasation.

Tibia (T), n (%)	Humerus (H), n (%)	Cardiac Arrest, n (%)	Trauma, n (%)	Insertion Success, n (%)	Insertion Time (s) (Mean)	Complications
9 (45)	11 (55)	Not reported	14 (70)	18 (90)	108	Two extravasations (humerus)
51 (98)	1 (2)	43 (74)	15 (26)	54 (90)	Not reported	None reported
77 (10)	0	41 (53)	15 (19)	75 (97)	Not reported	None reported
42 (100)	0	Not reported	21 (50)	39 (93)	Not reported	None reported
85 (75)	12 (11)	64 (67)	29 (27)	114 (100)	<30	None reported
Not specified	Not specified	55 (53)	Not reported	99 (94)	103.6	One compartment syndrome
Not specified	Not specified	30 (76)	Not reported	First: 33 (84) Second: 38 (97)	Not reported	None reported
64 (35)	51 (28)	115 (100)	None	T: 58 (91) H: 26 (51)	Not reported	5 (20%) humerus dislodgement
58 (66)	30 (34)	88 (100)	None	T: 52 (90) H: 18 (60)	Not reported	Six humerus and three tibia needle dislodgements
24 (69)	11 (31)	Not reported	8 (23)	35 (100)	All 35 <20 s	None reported
None	29 (100)	2 (7)	12 (40)	24 (80)	90	None reported
Not reported	Not reported	Not reported	30 (31)	89 (94)	77% in <10 s	One dislodgement One extravasation
89 (100)	0	Not reported	Not reported	78 (87)	Not reported	None reported
499 (55)	145 (16)	438 (46)	144 (16)	817/908 (90%)	60	19/908 (2.1%)

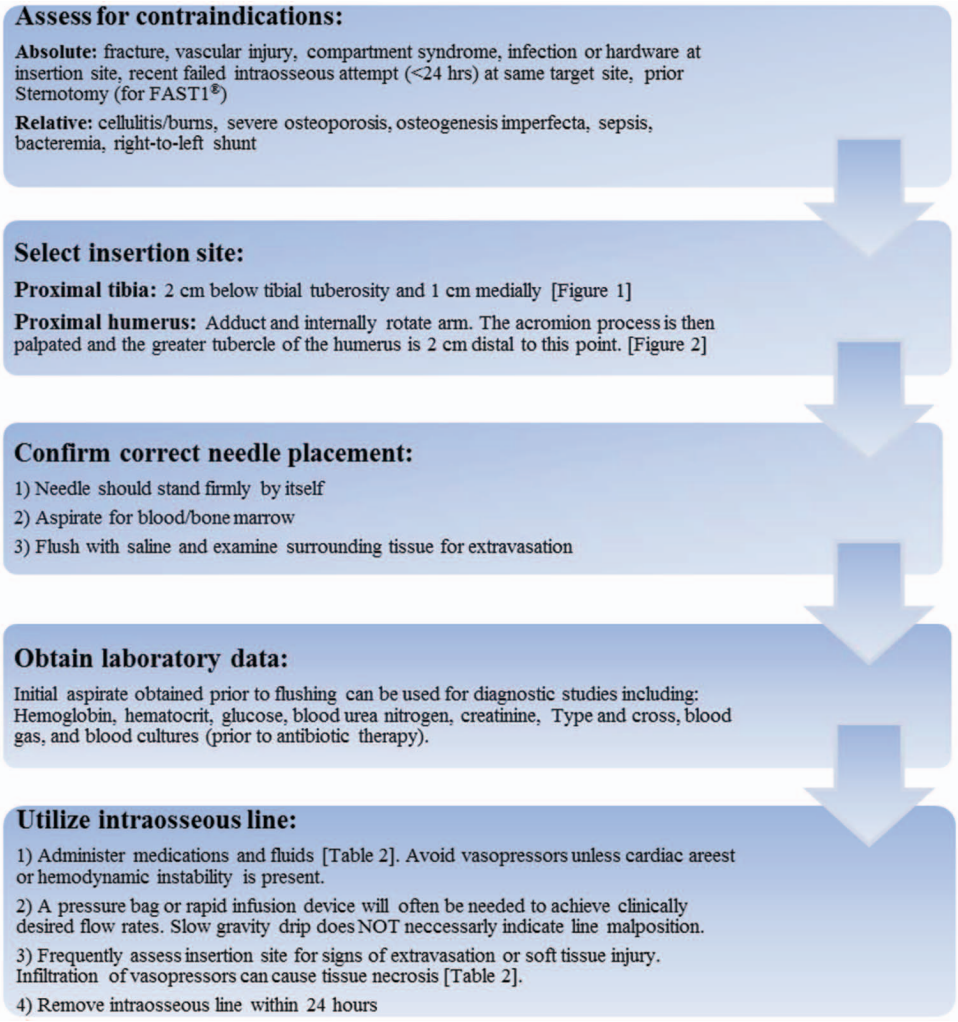

Fig. 8. A summary of intraosseous insertion and use in clinical practice. (FAST1®; Pyng Medical Corporation, Richmond, British Columbia, Canada.)

Alternatively, excessive length increases the risk of puncturing the posterior cortex leading to infusion of fluids into the deep compartments of the extremity.[102] As a result, some authors advocate using tissue thickness to determine proper needle size rather than relying on weight-based parameters.[7]

Compartment Syndrome

There have been at least eight published case reports of compartment syndrome secondary to intraosseous line extravasation.[103–110] Risk factors for developing compartment syndrome include: total fluid volume and infusion rate, bone fracture, needle dislodgement, fluid osmolarity (hypertonic saline), and recent cortical puncture in the same bone.[111] A compartment syndrome can potentially occur in the absence of technical errors. A canine study was conducted with 20-gauge intraosseous needles inserted surgically under direct visualization and cemented in place to eliminate the possibility of dislodgement or extravasation. Saline, with a radio-opaque dye, was infused at a rate of 480 ml/h. Serial radiographic examinations and compartment pressure measurements were performed. After 350 ml of fluid infusion, dye was detected in the surrounding soft tissue and compartment pressures increased to 35 mmHg. Compartment pressures continued to increase in direct proportion to the amount of dye injected leading the authors to conclude that a dose- and time-dependent scale for safe intraosseous infusion should be established in humans.[112]

Infection

There are several case reports from the 1940s detailing osteomyelitis attributable to intraosseous infusions. However, the incidence of infections from both intraosseous and intravenous infusions was similar during this time period suggesting poor sterile technique played a role in both groups. In 1985, a large review examining 30 studies and 4,270 patients concluded that there was a 0.6% incidence of osteomyelitis attributed to intraosseous use.[30] However, this meta-analysis predates the advent of new battery-powered intraosseous insertion devices (as well as modern day aseptic technique). In this review, zero infectious complications were reported in 1,367 total intraosseous insertions with modern devices (tables 3–5).

Embolic Complications

Fat or bone marrow embolism is another potential complication of intraosseous therapy. Even small increases in intraosseous pressure can lead to fat embolism.[113] Levels of radioactivity in the lungs were measured after injection of Triolein-^{131}I–labeled fat into the tibia of rabbits. After 2 to 5 h, 44.8% of the injected radioactive substance was present in the lungs on histologic examination.[113] More recently, Orlowski *et al.*[98] demonstrated that bone marrow and fat emboli in the lungs (mean, 0.91 emboli per square millimeter lung) were present in 89 to 100% of dogs after 4 h of intraosseous infusion. In addition, they demonstrated an average of 0.23 and 0.71 emboli per square millimeter lung, respectively, in pulmonary autopsy specimens of two children who received intraosseous infusions during resuscitation attempts. The incidence of fat embolism does not seem to be related to the rate of intraosseous infusion.[114]

The incidence of fat embolism after CPR with concurrent intraosseous infusion has been studied in a piglet model of hypoxic cardiac arrest. There was no statistically significant difference in the quantity of pulmonary emboli between the intraosseous and intravenous resuscitated groups.[115] These results correlate with recent human findings. Autopsies conducted on 50 decedents showed a pulmonary fat emboli rate of 76% in patients who received CPR without an intraosseous line.[116] These collective data suggest that patients undergoing CPR are at risk for pulmonary fat emboli with or without the presence of an intraosseous infusion.

Interestingly, despite the high percentage of fat and marrow emboli occurring with intraosseous infusions, there does not seem to be a detrimental clinical correlation. Despite an 89 to 100% incidence of emboli in his experiments, Orlowski *et al.*[98] found no significant alterations in Pa_{O_2} and no evidence of intrapulmonary shunting. There is at least a theoretical risk of cerebral emboli if right-to-left intracardiac shunts are present.[98] There is one case report of death from fat embolism after intraosseous phlebography to examine inferior vena cava obstruction in a patient with reticulum-cell sarcoma.[117] To date, however, there are no case reports of death or significant morbidity from marrow or fat emboli after resuscitation with an intraosseous infusion. Despite the near-universal occurrence of emboli, intraosseous infusions seem safe to use during resuscitation.

Bone Injury

There is a theoretical potential for both acute and long-term osseous injury related to intraosseous infusions. Bilateral tibia fractures were reported in a 3-month-old septic patient after unsuccessful intraosseous attempts.[118] Iatrogenic fracture has also been documented after aggressive intraosseous placement with "considerable force" during an unsuccessful resuscitation of a 2-yr-old trauma patient.[119] Overall, reports of fracture or acute boney injury attributable to intraosseous insertion are rare. Pig models have been used to demonstrate no long-term effects on bone marrow after intraosseous drug administration. Animals received sodium bicarbonate, epinephrine, and dopamine in one extremity while another extremity served as the control. Bone marrow examination revealed normal cellular differentiation in all groups.[120] In a similar study, experimental and control legs were harvested 6 months after intraosseous infusion. No differences in bone growth, degree of epiphyseal closure, or radiographic properties were observed between groups.[121] The rate or osmolality of intraosseous infusion does not appear to have an influence on long-term histologic changes of the marrow space in humans.[122]

Data from more recent human studies support the findings of these pig models. A prospective radiographic analysis of pediatric patients with tibial intraosseous infusions placed in emergency situations was conducted. After a mean follow-up period of 29.2 months, there was no statistically significant difference (in a variety of radiographic measurements) between the punctured and control legs.[123] Similarly, a small study (prospective, observer-blinded) found no difference in tibial length 1 yr after intraosseous infusion.[124] Given the rarity of iatrogenic fractures attributed to intraosseous cannulation and the lack of evidence showing adverse long-term bone growth effects, the intraosseous route seems to be low risk in terms of osseous complications.

Current Limitations

The available intraosseous literature has some limitations that must be considered. Most data come from prehospital or emergency department insertion. In this setting, intraosseous access is often used only after intravenous attempts have failed. As such, it is difficult to conduct large, randomized, clinical trials because the patients studied are already "self-selected" as difficult access patients. Therefore, we are left with primarily prospective observational studies. However, the findings of level III evidence were generally consistent in this review, allowing for a higher grade of recommendation.

Anesthesiologists frequently respond to in-hospital cardiac arrest situations, and literature specifically in this setting is scant. Head-to-head in-hospital studies comparing central and intraosseous access in terms of insertion speed and accuracy are lacking. There are no studies directly comparing the infection risks of the two routes when these lines are inserted during cardiac arrest. Furthermore, there are no studies comparing mortality data in cardiac arrest patients resuscitated with either central or intraosseous access.

Finally, long-term follow-up studies on the safety of intraosseous infusions are absent, particularly with newer insertion devices. Most of the recent literature tends to focus on speed and success of insertion. Therefore, we are left to rely on a few case reports and animal studies when considering the risk of delayed complications.

Conclusion

Intraosseous cannulation is a time-tested procedure that will play a role in the resuscitation of patients in the future. Intravenous access is often difficult to achieve in shock patients and central line placement can be time consuming. This literature review has demonstrated that intraosseous vascular

access can be achieved quickly and accurately in emergency situations. Given the efficiency of insertion combined with a favorable complication profile, there is clearly a role for intraosseous vascular access in the resuscitation of critically ill patients. Therefore, anesthesiologists should become familiar with intraosseous insertion techniques and understand how to properly use this potentially life-saving procedure. In the 1940s, Dr. Papper played an important early role in advancing the field of intraosseous infusions. Today, anesthesiologists have the opportunity to follow Dr. Papper's footsteps and be at the forefront of the intraosseous resurgence as we adopt this technique in our clinical practice.

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Competing Interests

The author declares no competing interests.

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References

1. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, Kudenchuk PJ, Ornato JP, McNally B, Silvers SM, Passman RS, White RD, Hess EP, Tang W, Davis D, Sinz E, Morrison LJ: Part 8: Adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010; 122(18 suppl 3):S729–67
2. Kern KB, Hilwig RW, Berg RA, Sanders AB, Ewy GA: Importance of continuous chest compressions during cardiopulmonary resuscitation: Improved outcome during a simulated single lay-rescuer scenario. Circulation 2002; 105:645–9
3. Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T: Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. N Engl J Med 1999; 341:871–8
4. Rittenberger JC, Menegazzi JJ, Callaway CW: Association of delay to first intervention with return of spontaneous circulation in a swine model of cardiac arrest. Resuscitation 2007; 73:154–60
5. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, Koster RW, Wyllie J, Böttiger B; ERC Guidelines Writing Group: European Resuscitation Council Guidelines for Resuscitation 2010 Section 1. Executive summary. Resuscitation 2010; 81:1219–76
6. Sackett DL: Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1989; 95(2 suppl):2S–4
7. Frascone RJ, Jensen J, Wewerka SS, Salzman JG: Use of the pediatric EZ-IO needle by emergency medical services providers. Pediatr Emerg Care 2009; 25:329–32
8. Ngo AS, Oh JJ, Chen Y, Yong D, Ong ME: Intraosseous vascular access in adults using the EZ-IO in an emergency department. Int J Emerg Med 2009; 2:155–60
9. Drinker CK, Drinker KR, Lund CC: The circulation in the mammalian bone marrow. Am J Physiol 1922; 62:1–92
10. Tocantins L: Rapid absorption of substances injected into the bone marrow. Proc Soc Exp Biol Med 1940; 45:292–6
11. Tocantins L, O'Neill J, Jones H: Infusion of blood and other fluids *via* the bone marrow: Applilcation in pediatrics. JAMA 1941; 117:1229–34
12. Papper EM: The Bone marrow route for injecting fluids *via* the bone marrow. ANESTHESIOLOGY 1942; 3:307–13
13. Bailey H: Bone-marrow as a site for the receprtion of infusions, trans-fusion and anesthetic agents. Br Med J 1944; 2:181–2
14. Dubick MA, Holcomb JB: A review of intraosseous vascular access: Current status and military application. Mil Med 2000; 165:552–9
15. Orlowski JP: My kingdom for an intravenous line. Am J Dis Child 1984; 138:803
16. Laroche M: Intraosseous circulation from physiology to disease. Joint Bone Spine 2002; 69:262–9
17. Tøndevold E, Eriksen J, Jansen E: Observations on long bone medullary pressure in relation to mean arterial blood pressure in the anaesthetized dog. Acta Orthop Scand 1979; 50:527–31
18. Banerjee S, Singhi SC, Singh S, Singh M: The intraosseous route is a suitable alternative to intravenous route for fluid resuscitation in severely dehydrated children. Indian Pediatr 1994; 31:1511–20
19. Leidel BA, Kirchhoff C, Bogner V, Stegmaier J, Mutschler W, Kanz KG, Braunstein V: Is the intraosseous access route fast and efficacious compared to conventional central venous catheterization in adult patients under resuscitation in the emergency department? A prospective observational pilot study. Patient Saf Surg 2009; 3:24
20. Fuchs S, LaCovey D, Paris P: A prehospital model of intraosseous infusion. Ann Emerg Med 1991; 20:371–4
21. Reades R, Studnek JR, Vandeventer S, Garrett J: Intraosseous *versus* intravenous vascular access during out-of-hospital cardiac arrest: A randomized controlled trial. Ann Emerg Med 2011; 58:509–16
22. Reiter DA, Strother CG, Weingart SD: The quality of cardiopulmonary resuscitation using supraglottic airways and intraosseous devices: A simulation trial. Resuscitation 2013; 84:93–7
23. Slovis CM, Herr EW, Londorf D, Little TD, Alexander BR, Guthmann RJ: Success rates for initiation of intravenous therapy en route by prehospital care providers. Am J Emerg Med 1990; 8:305–7
24. Jones SE, Nesper TP, Alcouloumre E: Prehospital intravenous line placement: A prospective study. Ann Emerg Med 1989; 18:244–6
25. Zuercher M, Kern KB, Indik JH, Loedl M, Hilwig RW, Ummenhofer W, Berg RA, Ewy GA: Epinephrine improves 24-hour survival in a swine model of prolonged ventricular fibrillation demonstrating that early intraosseous is superior to delayed intravenous administration. Anesth Analg 2011; 112:884–90
26. Mader TJ, Kellogg AR, Walterscheid JK, Lodding CC, Sherman LD: A randomized comparison of cardiocerebral and cardiopulmonary resuscitation using a swine model of prolonged ventricular fibrillation. Resuscitation 2010; 81:596–602
27. Niemann JT, Stratton SJ, Cruz B, Lewis RJ: Endotracheal drug administration during out-of-hospital resuscitation: Where are the survivors? Resuscitation 2002; 53:153–7
28. Marik PE, Flemmer M, Harrison W: The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: A systematic review of the literature and meta-analysis. Crit Care Med 2012; 40:2479–85

29. Smith JW, Egger M, Franklin G, Harbrecht B, Richardson JD: Central line-associated blood stream infection in the critically ill trauma patient. Am Surg 2011; 77:1038–42
30. Rosetti VA, Thompson BM, Miller J, Mateer JR, Aprahamian C: Intraosseous infusion: An alternative route of pediatric intravascular access. Ann Emerg Med 1985; 14:885–8
31. Leidel BA, Kirchhoff C, Braunstein V, Bogner V, Biberthaler P, Kanz KG: Comparison of two intraosseous access devices in adult patients under resuscitation in the emergency department: A prospective, randomized study. Resuscitation 2010; 81:994–9
32. Santos D, Carron PN, Yersin B, Pasquier M: EZ-IO(®) intraosseous device implementation in a pre-hospital emergency service: A prospective study and review of the literature. Resuscitation 2013; 84:440–5
33. Gazin N, Auger H, Jabre P, Jaulin C, Lecarpentier E, Bertrand C, Margenet A, Combes X: Efficacy and safety of the EZ-IO™ intraosseous device: Out-of-hospital implementation of a management algorithm for difficult vascular access. Resuscitation 2011; 82:126–9
34. Orlowski JP, Porembka DT, Gallagher JM, Lockrem JD, VanLente F: Comparison study of intraosseous, central intravenous, and peripheral intravenous infusions of emergency drugs. Am J Dis Child 1990; 144:112–7
35. Von Hoff DD, Kuhn JG, Burris HA III, Miller LJ: Does intraosseous equal intravenous? A pharmacokinetic study. Am J Emerg Med 2008; 26:31–8
36. Spivey WH, Crespo SG, Fuhs LR, Schoffstall JM: Plasma catecholamine levels after intraosseous epinephrine administration in a cardiac arrest model. Ann Emerg Med 1992; 21:127–31
37. Hoskins SL, do Nascimento P Jr, Lima RM, Espana-Tenorio JM, Kramer GC: Pharmacokinetics of intraosseous and central venous drug delivery during cardiopulmonary resuscitation. Resuscitation 2012; 83:107–12
38. Spivey WH: Intraosseous infusions. J Pediatr 1987; 111:639–43
39. Friedman FD: Intraosseous adenosine for the termination of supraventricular tachycardia in an infant. Ann Emerg Med 1996; 28:356–8
40. Goodman IS, Lu CJ: Intraosseous infusion is unreliable for adenosine delivery in the treatment of supraventricular tachycardia. Pediatr Emerg Care 2012; 28:47–8
41. Ruiz-Hornillos PJ, Martínez-Cámara F, Elizondo M, Jiménez-Fraile JA, Del Mar Alonso-Sánchez M, Galán D, García-Rubira JC, Macaya C, Ibanez B: Systemic fibrinolysis through intraosseous vascular access in ST-segment elevation myocardial infarction. Ann Emerg Med 2011; 57:572–4
42. Valdés M, Araujo P, de Andrés C, Sastre E, Martin T: Intraosseous administration of thrombolysis in out-of-hospital massive pulmonary thromboembolism. Emerg Med J 2010; 27:641–4
43. Joseph G, Tobias JD: The use of intraosseous infusions in the operating room. J Clin Anesth 2008; 20:469–73
44. Glaeser PW, Hellmich TR, Szewczuga D, Losek JD, Smith DS: Five-year experience in prehospital intraosseous infusions in children and adults. Ann Emerg Med 1993; 22:1119–24
45. Fiorito BA, Mirza F, Doran TM, Oberle AN, Cruz EC, Wendtland CL, Abd-Allah SA: Intraosseous access in the setting of pediatric critical care transport. Pediatr Crit Care Med 2005; 6:50–3
46. Paxton JH, Knuth TE, Klausner HA: Proximal humerus intraosseous infusion: A preferred emergency venous access. J Trauma 2009; 67:606–11
47. Guy J, Haley K, Zuspan SJ: Use of intraosseous infusion in the pediatric trauma patient. J Pediatr Surg 1993; 28:158–61
48. Buck ML, Wiggins BS, Sesler JM: Intraosseous drug administration in children and adults during cardiopulmonary resuscitation. Ann Pharmacother 2007; 41:1679–86
49. Brunette DD, Fischer R: Intravascular access in pediatric cardiac arrest. Am J Emerg Med 1988; 6:577–9
50. Kelsall AW: Resuscitation with intraosseous lines in neonatal units. Arch Dis Child 1993; 68(3 Spec No):324–5
51. Tarrow AB, Turkel H, Thompson MS: Infusions *via* the bone marrow and biopsy of the bone and bone marrow. Anesthesiology 1952; 13:501–9
52. Johnson L, Kissoon N, Fiallos M, Abdelmoneim T, Murphy S: Use of intraosseous blood to assess blood chemistries and hemoglobin during cardiopulmonary resuscitation with drug infusions. Crit Care Med 1999; 27:1147–52
53. Goldstein B, Doody D, Briggs S: Emergency intraosseous infusion in severely burned children. Pediatr Emerg Care 1990; 6:195–7
54. Berg RA: Emergency infusion of catecholamines into bone marrow. Am J Dis Child 1984; 138:810–1
55. Christensen DW, Vernon DD, Banner W Jr, Dean JM: Skin necrosis complicating intraosseous infusion. Pediatr Emerg Care 1991; 7:289–90
56. Walsh-Kelly CM, Berens RJ, Glaeser PW, Losek JD: Intraosseous infusion of phenytoin. Am J Emerg Med 1986; 4:523–4
57. Weiser G, Poppa E, Katz Y, Bahouth H, Shavit I: Intraosseous blood transfusion in infants with traumatic hemorrhagic shock. Am J Emerg Med 2013; 31:640.e3–4
58. Dubick MA, Kramer GC: Hypertonic saline dextran (HSD) and intraosseous vascular access for the treatment of haemorrhagic hypotension in the far-forward combat arena. Ann Acad Med Singapore 1997; 26:64–9
59. Chávez-Negrete A, Majluf Cruz S, Frati Munari A, Perches A, Argüero R: Treatment of hemorrhagic shock with intraosseous or intravenous infusion of hypertonic saline dextran solution. Eur Surg Res 1991; 23:123–9
60. Bell MC, Olshaker JS, Brown CK, McNamee GA Jr, Fauver GM: Intraosseous transfusion in an anesthetized swine model using ^{51}Cr-labeled autologous red blood cells. J Trauma 1991; 31:1487–9
61. Plewa MC, King RW, Fenn-Buderer N, Gretzinger K, Renuart D, Cruz R: Hematologic safety of intraosseous blood transfusion in a swine model of pediatric hemorrhagic hypovolemia. Acad Emerg Med 1995; 2:799–809
62. Kentner R, Haas T, Gervais H, Hiller B, Dick W: Pharmacokinetics and pharmacodynamics of hydroxyethyl starch in hypovolemic pigs; a comparison of peripheral and intraosseous infusion. Resuscitation 1999; 40:37–44
63. Neufeld JD, Marx JA, Moore EE, Light AI: Comparison of intraosseous, central, and peripheral routes of crystalloid infusion for resuscitation of hemorrhagic shock in a swine model. J Trauma 1993; 34:422–8
64. Miller LJ, Philbeck TE, Montez D, Spadaccini CJ: A new study of intraosseous blood for laboratory analysis. Arch Pathol Lab Med 2010; 134:1253–60
65. Orlowski JP, Porembka DT, Gallagher JM, Van Lente F: The bone marrow as a source of laboratory studies. Ann Emerg Med 1989; 18:1348–51
66. Brickman KR, Krupp K, Rega P, Alexander J, Guinness M: Typing and screening of blood from intraosseous access. Ann Emerg Med 1992; 21:414–7
67. Dolister M, Miller S, Borron S, Truemper E, Shah M, Lanford MR, Philbeck TE: Intraosseous vascular access is safe, effective and costs less than central venous catheters for patients in the hospital setting. J Vasc Access 2013; 14:216–24
68. Molin R, Hallas P, Brabrand M, Schmidt TA: Current use of intraosseous infusion in Danish emergency departments: A cross-sectional study. Scand J Trauma Resusc Emerg Med 2010; 18:37
69. Boon JM, Gorry DL, Meiring JH: Finding an ideal site for intraosseous infusion of the tibia: An anatomical study. Clin Anat 2003; 16:15–8
70. Lairet J, Bebarta V, Lairet K, Kacprowicz R, Lawler C, Pitotti R, Bush A, King J: A comparison of proximal tibia, distal femur, and proximal humerus infusion rates using the EZ-IO intraosseous device on the adult swine (Sus scrofa) model. Prehosp Emerg Care 2013; 17:280–4

71. Miller L, Philbeck T, Montez D, Puga T: 467: A two-phase study of fluid administration measurement during intraosseous infusion. Ann Emerg Med 2010; 56:S151
72. Ong ME, Chan YH, Oh JJ, Ngo AS: An observational, prospective study comparing tibial and humeral intraosseous access using the EZ-IO. Am J Emerg Med 2009; 27:8–15
73. Li SF, Cole M, Forest R, Chilstrom M, Reinersman E, Jones MP, Zinzuwadia S, King S, Yadav K: Are 2 smaller intravenous catheters as good as 1 larger intravenous catheter? Am J Emerg Med 2010; 28:724–7
74. Barcelona SL, Vilich F, Coté CJ: A comparison of flow rates and warming capabilities of the Level 1 and Rapid Infusion System with various-size intravenous catheters. Anesth Analg 2003; 97:358–63
75. Kalechstein S, Permual A, Cameron BM, Pemberton J, Hollaar G, Duffy D, Cameron BH: Evaluation of a new pediatric intraosseous needle insertion device for low-resource settings. J Pediatr Surg 2012; 47:974–9
76. Wagner MB, McCabe JB: A comparison of four techniques to establish intraosseous infusion. Pediatr Emerg Care 1988; 4:87–91
77. Jun H, Haruyama AZ, Chang KS, Yamamoto LG: Comparison of a new screw-tipped intraosseous needle *versus* a standard bone marrow aspiration needle for infusion. Am J Emerg Med 2000; 18:135–9
78. Miner WF, Corneli HM, Bolte RG, Lehnhof D, Clawson JJ: Prehospital use of intraosseous infusion by paramedics. Pediatr Emerg Care 1989; 5:5–7
79. Macnab A, Christenson J, Findlay J, Horwood B, Johnson D, Jones L, Phillips K, Pollack C Jr, Robinson DJ, Rumball C, Stair T, Tiffany B, Whelan M: A new system for sternal intraosseous infusion in adults. Prehosp Emerg Care 2000; 4:173–7
80. Miller DD, Guimond G, Hostler DP, Platt T, Wang HE: Feasibility of sternal intraosseous access by emergency medical technician students. Prehosp Emerg Care 2005; 9:73–8
81. Calkins MD, Fitzgerald G, Bentley TB, Burris D: Intraosseous infusion devices: A comparison for potential use in special operations. J Trauma 2000; 48:1068–74
82. Frascone RJ, Jensen JP, Kaye K, Salzman JG: Consecutive field trials using two different intraosseous devices. Prehosp Emerg Care 2007; 11:164–71
83. Byars DV, Tsuchitani SN, Erwin E, Anglemyer B, Eastman J: Evaluation of success rate and access time for an adult sternal intraosseous device deployed in the prehospital setting. Prehosp Disaster Med 2011; 26:127–9
84. Schwartz D, Amir L, Dichter R, Figenberg Z: The use of a powered device for intraosseous drug and fluid administration in a national EMS: A 4-year experience. J Trauma 2008; 64:650–4; discussion 654–5
85. Gerritse BM, Scheffer GJ, Draaisma JM: Prehospital intraosseus access with the bone injection gun by a helicopter-transported emergency medical team. J Trauma 2009; 66:1739–41
86. Olsen D, Packer BE, Perrett J, Balentine H, Andrews GA: Evaluation of the bone injection gun as a method for intraosseous cannula placement for fluid therapy in adult dogs. Vet Surg 2002; 31:533–40
87. Brenner T, Bernhard M, Helm M, Doll S, Völkl A, Ganion N, Friedmann C, Sikinger M, Knapp J, Martin E, Gries A: Comparison of two intraosseous infusion systems for adult emergency medical use. Resuscitation 2008; 78:314–9
88. Sunde GA, Heradstveit BE, Vikenes BH, Heltne JK: Emergency intraosseous access in a helicopter emergency medical service: A retrospective study. Scand J Trauma Resusc Emerg Med 2010; 18:52
89. Levitan RM, Bortle CD, Snyder TA, Nitsch DA, Pisaturo JT, Butler KH: Use of a battery-operated needle driver for intraosseous access by novice users: Skill acquisition with cadavers. Ann Emerg Med 2009; 54:692–4
90. Shavit I, Hoffmann Y, Galbraith R, Waisman Y: Comparison of two mechanical intraosseous infusion devices: A pilot, randomized crossover trial. Resuscitation 2009; 80:1029–33
91. Schalk R, Schweigkofler U, Lotz G, Zacharowski K, Latasch L, Byhahn C: Efficacy of the EZ-IO needle driver for out-of-hospital intraosseous access—A preliminary, observational, multicenter study. Scand J Trauma Resusc Emerg Med 2011; 19:65
92. Tan BK, Chong S, Koh ZX, Ong ME: EZ-IO in the ED: An observational, prospective study comparing flow rates with proximal and distal tibia intraosseous access in adults. Am J Emerg Med 2012; 30:1602–6
93. Torres F, Galán MD, Alonso Mdel M, Suárez R, Camacho C, Almagro V: Intraosseous access EZ-IO in a prehospital emergency service. J Emerg Nurs 2013; 39:511–4
94. Reades R, Studnek JR, Garrett JS, Vandeventer S, Blackwell T: Comparison of first-attempt success between tibial and humeral intraosseous insertions during out-of-hospital cardiac arrest. Prehosp Emerg Care 2011; 15:278–81
95. Horton MA, Beamer C: Powered intraosseous insertion provides safe and effective vascular access for pediatric emergency patients. Pediatr Emerg Care 2008; 24:347–50
96. Luck RP, Haines C, Mull CC: Intraosseous access. J Emerg Med 2010; 39:468–75
97. LaRocco BG, Wang HE: Intraosseous infusion. Prehosp Emerg Care 2003; 7:280–5
98. Orlowski JP, Julius CJ, Petras RE, Porembka DT, Gallagher JM: The safety of intraosseous infusions: Risks of fat and bone marrow emboli to the lungs. Ann Emerg Med 1989; 18:1062–7
99. Orlowski JP: Emergency alternatives to intravenous access. Intraosseous, intratracheal, sublingual, and other-site drug administration. Pediatr Clin North Am 1994; 41:1183–99
100. Hansen M, Meckler G, Spiro D, Newgard C: Intraosseous line use, complications, and outcomes among a population-based cohort of children presenting to California hospitals. Pediatr Emerg Care 2011; 27:928–32
101. Paxton JH: Intraosseous vascular access: A review. J Trauma 2012; 14:195–32
102. LaSpada J, Kissoon N, Melker R, Murphy S, Miller G, Peterson R: Extravasation rates and complications of intraosseous needles during gravity and pressure infusion. Crit Care Med 1995; 23:2023–8
103. Atanda A Jr, Statter MB: Compartment syndrome of the leg after intraosseous infusion: Guidelines for prevention, early detection, and treatment. Am J Orthop (Belle Mead NJ) 2008; 37:E198–200
104. Moen TC, Sarwark JF: Compartment syndrome following intraosseous infusion. Orthopedics 2008; 31:815
105. Galpin RD, Kronick JB, Willis RB, Frewen TC: Bilateral lower extremity compartment syndromes secondary to intraosseous fluid resuscitation. J Pediatr Orthop 1991; 11:773–6
106. Gayle M, Kissoon N: A case of compartment syndrome following intraosseous infusions. Pediatr Emerg Care 1994; 10:378
107. Moscati R, Moore GP: Compartment syndrome with resultant amputation following intraosseous infusion. Am J Emerg Med 1990; 8:470–1
108. Ribeiro JA, Price CT, Knapp DR Jr: Compartment syndrome of the lower extremity after intraosseous infusion of fluid. A report of two cases. J Bone Joint Surg Am 1993; 75:430–3
109. Vidal R, Kissoon N, Gayle M: Compartment syndrome following intraosseous infusion. Pediatrics 1993; 91:1201–2
110. Wright R, Reynolds SL, Nachtsheim B: Compartment syndrome secondary to prolonged intraosseous infusion. Pediatr Emerg Care 1994; 10:157–9
111. Alam HB, Punzalan CM, Koustova E, Bowyer MW, Rhee P: Hypertonic saline: Intraosseous infusion causes myonecrosis in a dehydrated swine model of uncontrolled hemorrhagic shock. J Trauma 2002; 52:18–25

112. Günal I, Köse N, Gürer D: Compartment syndrome after intraosseous infusion: An experimental study in dogs. J Pediatr Surg 1996; 31:1491–3
113. Whitenack SH, Hausberger FX: Intravasation of fat from the bone marrow cavity. Am J Pathol 1971; 65:335–45
114. Hasan MY, Kissoon N, Khan TM, Saldajeno V, Goldstein J, Murphy SP: Intraosseous infusion and pulmonary fat embolism. Pediatr Crit Care Med 2001; 2:133–8
115. Fiallos M, Kissoon N, Abdelmoneim T, Johnson L, Murphy S, Lu L, Masood S, Idris A: Fat embolism with the use of intraosseous infusion during cardiopulmonary resuscitation. Am J Med Sci 1997; 314:73–9
116. Eriksson EA, Pellegrini DC, Vanderkolk WE, Minshall CT, Fakhry SM, Cohle SD: Incidence of pulmonary fat embolism at autopsy: An undiagnosed epidemic. J Trauma 2011; 71:312–5
117. Thomas ML, Tighe JR: Death from fat embolism as a complication of intraosseous phlebography. Lancet 1973; 2:1415–6
118. La Fleche FR, Slepin MJ, Vargas J, Milzman DP: Iatrogenic bilateral tibial fractures after intraosseous infusion attempts in a 3-month-old infant. Ann Emerg Med 1989; 18:1099–101
119. Bowley DM, Loveland J, Pitcher GJ: Tibial fracture as a complication of intraosseous infusion during pediatric resuscitation. J Trauma 2003; 55:786–7
120. Pollack CV Jr, Pender ES, Woodall BN, Tubbs RC, Iyer RV, Miller HW: Long-term local effects of intraosseous infusion on tibial bone marrow in the weanling pig model. Am J Emerg Med 1992; 10:27–31
121. Woodall BN, Pender ES, Pollack CV Jr, Miller H, Tubbs RC, Andrew ME: Intraosseous infusion of resuscitative fluids and drugs: Long-term effect on linear bone growth in pigs. South Med J 1992; 85:820–4
122. Brickman KR, Rega P, Schoolfield L, Harkins K, Weisbrode SE, Reynolds G: Investigation of bone developmental and histopathologic changes from intraosseous infusion. Ann Emerg Med 1996; 28:430–5
123. Claudet I, Baunin C, Laporte-Turpin E, Marcoux MO, Grouteau E, Cahuzac JP: Long-term effects on tibial growth after intraosseous infusion: A prospective, radiographic analysis. Pediatr Emerg Care 2003; 19:397–401
124. Fiser RT, Walker WM, Seibert JJ, McCarthy R, Fiser DH: Tibial length following intraosseous infusion: A prospective, radiographic analysis. Pediatr Emerg Care 1997; 13:186–8

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Hasbrouck's Advertising "Proposal" for "Use of Nitrous Oxide"

Eventually notorious as the dentist-anesthetist for the secret shipboard surgery in 1893 to treat U.S. President Grover Cleveland's oral cancer, Dr. Ferdinand Hasbrouck was one of many professionals who shared use of this same stock illustration (*above*), an image copyrighted by A. B. Frenzel in 1881. Sadly, Dr. Hasbrouck failed to center his personal stamping (*lower right*), which advertised that teeth were "extracted without pain by the use of Nitrous Oxide Gas, a specialty." Depicting a broom-wielding lady menacing a young man proposing marriage to her rival or relative, this trade card is part of the WLM's Ben Z. Swanson Collection. (Copyright © the American Society of Anesthesiologists, Inc.)

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