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Bone Marrow Harvest: A White Paper of Best Practices by the NMDP Marrow Alliance

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Abstract

Data on recent bone marrow harvest (BMH) collections from the NMDP has shown that bone marrow (BM) quality has decreased based on total nucleated cell count in the product. To ensure that quality BM products are available to all recipients, the NMDP Marrow Alliance was formed in April 2021 to increase the capability of BM collection centers to safely deliver high-quality

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SUPPLEMENTARY MATERIALS

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products consistently and to identify and disseminate guidelines for performing BMH. This white paper describes the best practices for BMH as defined by the NMDP Marrow Alliance.

Keywords

Bone marrow; Harvest; Donor; Allogeneic

INTRODUCTION

Allogeneic hematopoietic cell transplantation (alloHCT) is a life-saving procedure for a variety of devastating diseases. NMDP was established in 1987 to facilitate alloHCT from anonymous volunteer adult unrelated donors (URDs) to patients in need. Bone marrow (BM) has been used as a source of hematopoietic stem cells (HSCs) from the 1960s [1] and is collected via a BM harvest (BMH) procedure. Although there has been a significant decrease in the use of BM as a stem cell source since the advent of granulocyte colony-stimulating factor-mobilized peripheral blood stem cell (PBSC) grafts [2,3], BM still accounts for 11% of total NMDP products provided and remains a crucial graft source. The decreased frequency of BM collections has the potential to impact the quality of BMH owing to several factors, including limited expertise in the technique and inadequate training of staff.

One important measure of BM quality is the cell dose collected and infused. A study by the Center for International Blood and Marrow Transplant Research (CIBMTR) examined the mean total nucleated cell (TNC) concentration in >15,000 BM donations collected at NMDP centers between 1994 and 2016 [4]. The investigators found a significant decline in the quality of the BM products in more recent eras, based on mean TNC concentration, which declined from 21.8×10^6 cells/mL in the earliest era (1994 to 1996) to 18.7×10^6 cells/mL in the most recent era (2012 to 2016) (means ratio, .83; $P < .001$). Moreover, multivariate regression analysis of the data showed that higher-volume centers (performing >30 collections per era) had better-quality harvests, suggesting that experience matters. Multiple studies have shown the importance of cell dose for patient outcomes [5–7]; thus, obtaining high-quality BM products remains of paramount importance.

Data on recent BM collections from the NMDP also support the decline in BM quality (unpublished data). To ensure the availability of high-quality BM products for all recipients, the NMDP Marrow Alliance (Alliance) was formed in April 2021 to increase the capability of BM collection centers (CCs) to safely deliver high-quality products consistently and to identify and disseminate the best practices for performing BMHs. The Alliance comprises NMDP BM CCs that demonstrate a commitment to serving the needs of recipients and donors while providing high-quality BM grafts. Alliance members include the following institutions: Medstar Georgetown University Hospital (Washington, DC), Brigham and Women's Hospital (Boston, MA), City of Hope (Duarte, CA), University of Washington/Fred Hutchinson Cancer Center (Seattle, WA), Mass General (Boston, MA), Ohio State University (Columbus, OH), Scripps (La Jolla, CA), and Vanderbilt University Medical Center (Nashville, TN).

One goal of the Alliance was to have the majority of NMDP URD BMHs performed at Alliance centers. More than two-thirds (69%) of domestic URD BMHs were performed at Alliance CCs in 2022. The NMDP had set a goal TNC dose of $3.0 \times 10^8/\text{kg}$ recipient weight as a quality metric for BM products in all recipients based on NMDP/CIBMTR internal data, as well as on previously published data [5,6]. In 2022, this dose was achieved 81% of the time at Alliance CCs, compared to 58% at non-Alliance CCs.

Discrepancies between recipient weight and donor weight may pose challenges to obtaining a quality BM product. NMDP evaluated the success of BMH based on 10-kg differences in recipient and donor weight in Alliance CCs and other CCs, using $3.0 \times 10^8/\text{kg}$ TNCs as the goal dose. As shown in Figure 1, when the recipient weighed ≥ 10 kg more than the donor, Alliance CCs were able to achieve this dose 43% of the time, compared with 25% for other CCs. This success rate improved to 65% in Alliance CC BM products and 42% in BM products from other CCs when the weight discrepancy was within 10 kg and was the best when the donor weight was ≥ 10 kg greater than the recipient weight (89% for Alliance CCs versus 80% for other CCs). We next evaluated the BM product quality based on recipient weight alone. BM product quality dropped significantly ($<50\%$) when the recipient weighed >70 kg (Table 1). Alliance CCs were more adept than other CCs at collecting a quality product in recipients weighing >70 kg based on the median TNC dose per recipient weight.

To improve BMH quality throughout the NMDP BM CC network, the Alliance held a summit on June 8 and 9, 2022, to explore best practices for BMH. This white paper describes these best practices as defined by the Alliance.

BMH TEAM

Based on current standards of the Foundation for Accreditation of Cellular Therapies (FACT), at least 1 BMH shall have been performed in the 12-month period immediately preceding initial accreditation, and a minimum average of 1 BMH per year shall be performed within each accreditation cycle at an accredited BM CC. The FACT standards address only the Medical Director's experience in performing BMHs and state that the director shall have performed or supervised a minimum of 10 BMHs during their career. The standards do not address the composition of the BMH team, the number of collections performed by each individual, staff training, or collection technique. Based on recommendations from the Alliance, the team should comprise the following members (with their respective roles): anesthesiologist (donor sedation, intraoperative analgesia, and airway management); scrub technician or nurse (sterile activities), circulating nurse (non-sterile activities); collection team, comprising either 2 collecting physicians or a collecting physician and an advanced practice provider (proceduralist who performs the BMH) and a technician (who handles the BM product). Of note, some CCs have the scrub technician handle the BM product as well as perform sterile activities. BMH proceduralists must maintain credentialing according to their institutional policy.

Recommendation:

The BM collection team plays a vital role in achieving high-quality BM products. Understanding the role each team member plays and communication throughout the procedure are keys to success.

DONOR COMMUNICATION**Pre-BMH Donor Review**

Once an individual has been cleared for BMH, they will receive information on what they can expect on the day of BMH, including skin cleaning and preparation, logistical details, and fasting guidelines. Additionally, dedicated time should be allotted to discuss the BMH procedure in detail. Some CCs may schedule a separate visit for this discussion close to the day of the procedure, whereas other CCs will hold this discussion on the day of collection. The purpose of the pre-BMH donor review is to (1) provide detailed information on the BMH, including any potential adverse events or complications; (2) obtain informed consent for the BMH; and (3) confirm that the donor eligibility and suitability status (previously obtained) are up to date. The expected events in the procedure/operating room prior to anesthesia and intubation are explained, the harvesting procedure itself is described, and the postprocedure evaluation to determine the suitability for discharge or the need for hospital admission overnight is outlined. Ideally, the donor's planned caregiver can be present for this discussion, but if not, an alternative time to discuss postprocedure wound management with the caregiver should be sought.

Consent for BMH

Potential adverse events secondary to BMH, as well as potential risks in the event that the donor requires a blood transfusion, should be discussed. Consent for type of anesthesia and intubation may be obtained at the same time as the pre-BMH donor consent; however, in some centers, it is obtained separately by an experienced anesthesia team at another time before the BMH.

A recommended approach to reviewing the risks and potential complications of BMH via a thorough step-by-step explanation of the process from the time of anesthesia and/or intubation through extubation of the donor. An anatomic model of the pelvis or equivalent anatomic diagram of the pelvis is a helpful tool for explanation purposes. The donor should understand that they will be in the prone position and be reassured that sterile technique will be maintained to reduce the risks of product contamination and superficial or deep infection of soft tissue or bone. This should include skin cleansing with appropriate antimicrobial agents and the use of other barrier methods, such as an Ioban dressing. The potential for soft tissue and musculoskeletal injury, including pain, swelling, bruising, bleeding, and hematoma, as well as infections, should be discussed, as should potential complications that could lead to neurologic sequelae, such as neuropathies, including the rare complication of inadvertent entry into the thecal sac, which may contribute to postprocedure headache.

The known risks of standard BMH have been published previously [8–16], and possible complications are listed in Table 2.

Blood Consent

Consent for peri-BMH blood component support should be discussed with the donor when obtaining informed consent prior to the BMH. The associated procedural blood loss can be roughly calculated to determine the likely post-BMH hematocrit (Hct) concentration (see example below). The anticipated volume of BM to be collected should be determined and discussed with the donor during the pre-BMH review. The volume of BM to be collected is usually in the range of 10 to 15 mL/kg of recipient weight; however, larger-volume BMH may be required for some protocols. Alternatively, a TNC dose, often corrected for the donor's WBC count, may serve as a goal for BMH. When a TNC dose is established as the goal for BMH, the anticipated BM volume can be estimated based on either the CC's expected average BM TNC count or the NMDP predicted median TNC count of $0.183 \times 10^8/\text{mL}$. The NMDP and many CCs limit the maximum volume collected to 20 mL/kg donor weight [17], although some centers will collect to a maximum of 1500 mL.

The associated blood loss can be roughly calculated to determine the likely post-BMH Hct level; a sample calculation is shown in Table 3. Assume that the Hct of the BM product will be roughly 30% (ie, 300 mL RBC volume loss per liter of BM harvested), and that the patient may lose a unit of blood into the soft tissues for each liter of BM harvested. The threshold at which the donor likely would require a blood transfusion should be discussed. At one author's center, for example, the threshold for post-BMH transfusion in healthy adult BM donors is a Hct $\leq 21\%$. Irradiated, allogeneic blood transfusions should be available in the event of significant blood loss. The donor should be made aware of potential risks of receiving allogeneic blood, including infection, and informed of the laboratory and/or clinical parameters that may indicate the need for transfusion.

Preoperative Autologous Blood Donation prior to BMH: Pros and Cons

The use of preoperative autologous blood donation (PAD) prior to BMH was a popular approach in the 1980s and early 1990s to mitigate transmissible diseases from allogeneic blood transfusions, such as HIV and hepatitis [18,19]. This approach was used initially for elective surgical procedures with moderate-to-high blood loss and has been shown to reduce exposure to allogeneic blood while potentially stimulating erythropoietin secretion and increasing erythropoiesis [20]. However, this effect on erythropoietin levels is modest at best and is seen only after donation of 3 to 4 units of blood at short intervals (eg, 2 units/week) [21]. At the height of its popularity, PAD was introduced for use in volunteer BM donation. The recommendation that volunteer BM donors be given the option of donating their own blood prior to BMH was incorporated into the guidelines for allogeneic HSC transplantation of several organizations, including the Australian Bone Marrow Donor Registry [22], the Eastern Cooperative Oncology Group [23], and the British Committee for Standards in Hematology [23]. The World Marrow Donor Association and NMDP produced guidelines stating that all BMH centers should collect preoperative autologous blood for transfusion back into volunteer donors during or after their BMH [24–27].

The practice of PAD has been called into question recently. In a retrospective study evaluating the cost-effectiveness of PAD in 61 BM donors, the mean hemoglobin (Hb) concentration fell from 12.9 g/dL to 11.8 g/dL in women who predonated 1 unit and from 13.2 g/dL to 10.9 g/dL those who predonated 2 units [28]. BMH led to a further decline in Hb concentration by 2.3 g/dL in women and by 2.4 g/dL in men. The post-BMH Hb fell to <9.0 g/dL in 39% of female donors and 6% of the male donors, all but 1 of whom had pre-donated blood. Similarly, another study found among 495 adult BM donors to adult recipients, 79% received an autologous transfusion, the median total volume of BM harvested was 900 mL (range, 450 to 1350 mL), and the median number of nucleated cells harvested was 3.2×10^8 /kg recipient weight (range, .9 to 7.4×10^8 /kg) [29]. The postdonation Hb was <8.5 g/dL in 4 donors and <9.0 g/dL in 25 donors. Of the 25 donors with post-harvest Hb <9.0 g/dL, 23 were females and 14 had received an autologous transfusion. Investigators found that postdonation Hb concentrations did not decrease to levels detrimental to healthy persons irrespective of whether or not autologous blood is transfused. This practice of PAD also carries risks [30], including the risk of incorrect blood transfusion, volume overload, bacterial contamination of blood [31], and errors in the handling and identification of blood bags. The postponement of planned transplantation may render the stored units useless, and the collection of autologous blood, reducing the Hb concentration in the donor prior to BMH, are also of concern. Importantly, the utilization rate of autologous units among BM donors was 45.6% overall, with 55% of women and 24% of men receiving autologous blood. In females, the percentage of transfused autologous units with a donor Hb of >9.0 g/dL was 59% in females and 71% in males [28]. Another study found similar mean baseline Hb values among BM donors who donated 1 or 2 units at 3 time points: before PAD collection, the morning before BMH, and shortly after BMH. However, after PAD collection, a more significant Hb drop was seen in the group that donated 2 units ($P = .045$), although after BMH, Hb levels were similar in the 2 groups; 61.2% of all donors required autologous transfusion, and none required allogeneic transfusion [31]. A baseline Hb <14.35 g/dL was identified as the sensitive cutoff to predict the need for transfusion after BMH (sensitivity, 52%; specificity, 80.4%; $P = .001$) [31]. A retrospective study examining 7024 BM donors from the CIBMTR database found that 60% received at least 1 unit of autologous blood [32]. The donors who received autologous blood were older and had a lower Hb preharvest, a longer duration of anesthesia, and a higher-volume BMH. Only donors who underwent high-volume BMH, defined as a BMH volume >27% of blood volume, benefited from autologous transfusion [32].

In summary, the use of PAD in healthy BM volunteers is becoming increasingly difficult to justify. A reduced risk of allogeneic transfusion-transmitted infection with similar rates of more common transfusion-related reactions, the lack of data on cost-effectiveness, and increasing anemia tolerance with reduced transfusion thresholds mean that this practice in healthy BM donors no longer may be necessary. Moreover, the coordination of preharvest autologous donation is logistically demanding and more costly than allogeneic blood on a cost-per-unit basis. In addition, one-third of autologous blood is wasted, compared to 7.4% of allogeneic blood [22]. Finally, the benefit of PAD can be realized only with an adequate interval between PAD and BMH, which usually is technically difficult considering the short time between BMH and infusion into the intended recipient. Further studies are needed to

better define parameters for PAD in healthy BM donors, including the use of nontransfusion alternatives, such as preoperative iron or erythropoietin. We recommend that PAD prior to BMH not be routinely offered to BM donors, and that physicians be educated about the shifting risk-benefit balance associated with autologous transfusion.

Recommendation:

PAD should NOT be routinely collected prior to a BMH. If a PAD unit has been made available, the transfusion of the collected product during or after the BMH should be based on clinical need only and should not routinely be given back to the donor.

Consent for Anesthesia and Intubation

In some CCs, the anesthesia team reaches out to the donor before the day of BMH to provide recommendations, discuss medication management, and even obtain consent for anesthesia and intubation, whereas in other CCs, the anesthesia team may do so shortly before the harvesting procedure. Some CCs may incorporate the consent for anesthesia and intubation at the same time when obtaining consent for the harvesting procedure. Individuals obtaining consent should discuss the nature of the planned anesthesia and any potential adverse events or risk from anesthesia and intubation. Common or rare complications include nausea, syncope, sore throat, chipped teeth, spinal headache (where appropriate), hypotension, myocardial infarction, anaphylaxis, prolonged paralysis after anesthesia, pulmonary embolism, malignant hyperthermia, pulmonary edema, significant arrhythmias, and stroke. Premedication may be offered to the donor once all consents are obtained.

Recommendation:

Donor consent should include the anesthesia type, BMH and the potential need for transfusion of any blood product.

ANESTHESIA

The preferred method of anesthesia for BMH is general anesthesia with intubation and ventilation. In fact, >99% of BMH volunteer URDs undergo general anesthesia (NMDP data, unpublished). This method is the safest for control the airways and ventilation of patients in the prone position [33], especially donors with airway management challenges (eg, obesity, asthma). Regional anesthesia using a spinal block for shorter and epidural anesthesia for longer cases can be used as an alternative; however, general anesthesia is the safest and most preferred method [34].

For the BMH, it is recommended that 2 i.v. catheters be placed for intraoperative fluid management, with infusion adjusted in real time based on the BMH volume collected. Withdrawn BM should be replaced i.v. with a crystalloid solution, such as Ringer's lactate, at a 2:1 ratio during the procedure and an additional volume aliquot after-ward, for a total replacement volume of 3:1. Because BM withdrawal can occur rapidly, prehydration with

500 or 1000 mL of crystalloid solution can be initiated in the preoperative preparation area. Donors receiving regional anesthesia benefit from an additional 500 mL of crystalloid solution prior to the procedure to counteract the effects of sympathicolysis related to the anesthesia [34]. During larger BM collections, parts of the 2:1 crystalloid fluid replacement may be substituted with a 1:1 colloid replacement using 5% albumin solution to limit the total fluid volume given during the procedure. It is important for the harvest team to communicate with anesthesia at several points before and during the procedure to coordinate and optimize the donor's care (Table 4).

Intraoperative hypotension is a frequent occurrence during BMH, especially when larger volumes of BM are withdrawn rapidly. Proactive fluid resuscitation management through 2 i.v. lines usually can prevent significant blood pressure fluctuations. Pressors such as phenylephrine or ephedrine may be used intraoperatively according to the judgment of the anesthetist; however, the associated vasoconstriction may affect stem cell yield negatively. In addition, the donor's prone position on the operating table typically generates an enhanced response to pressors, potentially leading to greater blood pressure fluctuations [35].

Typically, the withdrawal of 30% of the donor's total estimated blood volume leads to a decrease in Hb of up to 5 g/dL (~1 g/dL for each 300 mL) of BM collected, independent of the preprocedure Hb level [29,36]. Although this will render most donors mildly anemic, transfusion thresholds of ≤ 7 g/dL will be breached only in donors with a preprocedure Hb level < 12 g/dL. Strategies to prevent the need for unnecessary postprocedure transfusion could include limiting BM collection volumes to 30% (for female donors) or 33% (for male donors) of estimated donor blood volume up to a maximum of 1500 mL, correcting preprocedure anemia with iron supplementation in known hypoferritinemic donors (such as young menstruating women), and providing iron supplementation to all donors for at least 1 month after the procedure [28].

BMH PROCEDURE

Optimal instrument choice, operating room setup, and site selection tailored to the donor, the requested product, and the procedural team will promote safe and efficient BMH.

BM Needle

Commercially available BM needle systems vary in key parameters relating to trocar, stylet, and handle features (Tables 5 and A1). No single product fits every purpose or is used by every expert operator. For most adult donors, needle size and handle characteristics have the greatest impact on a harvester's subjective experience.

Needle Length—A needle length of roughly 10 cm allows for extended penetration into the medullary space of the posterior superior iliac spine (PSIS) in most adult donors while also permitting consistent application of axial force during trocar rotation to engage the iliac cortex. Needles shorter than 8 cm can function effectively for particularly thin or pediatric donors but may lack sufficient penetration in adult donors of at least average body habitus, particularly for second, deeper passes at each aspiration site. Needles longer than 10 cm may be necessary for donors with thick (> 5 cm) subcutaneous tissue overlying the posterior

iliac bones. However, length comes at the expense of control over the tip while engaging the cortex. This issue is magnified when extending the harvest from the PSIS superiorly along the much narrower iliac crest, where the risk of needle slippage causing soft tissue trauma is greater.

Recommendation:

A needle length of approximately 10 cm suits most adult donors. Longer needles are reasonable for donors with thick subcutaneous tissue but require greater dexterity.

Handle Characteristics—An ergonomic handle with sufficient surface area through which to apply force during needle insertion and stylet extraction will promote sustained harvesting efficiency even with prolonged procedures. In this regard, twist-lock T-shaped stylet handles that engage flush with the trocar handle during BM insertion and are rotated 90 degrees for extraction distribute manual forces over broad areas of the palm and fingers, respectively. Nontwist T-shaped stylet handles that leave a gap with the trocar handle or have another contact surface for stylet extraction may provide a similar level of comfort. Stylets with recessed, nontwist handles that are flush with the trocar handle can become difficult to dislodge, particularly after many passes through the cortex; doing so can require manual prying, which may cause discomfort in operators' hands.

Recommendation:

Stylets with a twist-lock handle, a gap between the stylet and trocar handles, or a prominent stylet handle grip will promote operator comfort during longer harvests.

Trocar Gauge—Commercially available trocars range from 8 gauge to 15 gauge, with 11 and 13 gauge the sizes used most frequently. These sizes balance the competing priorities of cortical penetration and (theoretically) faster bone healing with smaller-gauge trocars with the more rapid BM aspiration and reduced shear stress on HSCs during aspiration with larger-gauge trocars. The 11 gauge trocar needle strikes an excellent balance in most circumstances.

Trocar Tip—The tip of many harvest needles has a single bevel with an acute angle to create a broad, oblique orifice through which BM is aspirated. Some harvest needle tips have 2 or more bevels to facilitate advancing deeper into the medullary bone, with a smaller, more circular orifice. Single-bevel needles are very well suited for BMH given the importance of efficient aspiration, more so than drilling into bone, as would be the case for core biopsies. Of note, rotating the needle during aspiration to draw in virgin BM from 360 degrees around the tip may reduce hemodilution for single-bevel trocars lacking barrel fenestrations.

Recommendation:

Single-bevel, narrow angle trocar tips facilitate efficient BM aspiration but require rotation in absence of barrel fenestrations.

Trocar Barrel Fenestrations—Some BM needles have fenestrations spaced around the circumference of the trocar for intake of BM from all lateral directions in addition to the tip. This may reduce hemodilution resulting from sustained aspiration from a single focal point. Fenestrations are more commonly present in multi-beveled trocars lacking an oblique orifice.

Recommendation:

Trocar barrel fenestrations may reduce hemodilution with multi-beveled trocars; they promote a similar effect to rotation of trocars with single bevel tips.

Stylet Tip—Most BM needles have a stylet with a tapered, pyramidal tip to promote penetration through the iliac bone. Minor variations in shape exist, but all share a sharpened tip to engage the bony cortex and facilitate smooth advancement through the medullary space.

Recommendation:

A sharpened, tapered stylet tip will facilitate cortical engagement and penetration.

Site Selection

The bilateral PSIS harbor a high concentration of highly accessible BM. These structures can be identified as broadened bony surfaces while palpating medially and inferiorly along the posterior superior iliac crests (PSIC; Figure 2). By surface anatomy, the PSIS are typically located 5 to 8 cm equidistant in the superior and lateral directions from the superior margin of the gluteal cleft. They are readily identified even in donors with thick subcutaneous tissue given the absence of more superficial muscle tissue. (The gluteus medius and maximus muscles originate on the inferolateral edges of the PSIS and PSIC.)

Alternative Sites—BM also can be aspirated from the PSIC bilaterally. We resort to these secondary sites when BM aspiration from the PSIS wanes. The rare individuals in whom neither the iliac spines nor the crests are readily palpable should be identified in advance, during the initial donor physical examination, to allow for evaluation of prospective tertiary sites.

Safety Considerations—It is important to restrict needle passes to the areas superior and lateral from the iliac spines and to avoid passes inferior or medial to these landmarks. The latter areas encompass the sacroiliac joints and the sacral nerve roots that converge in the lumbosacral nerve trunk and, more distally, the sciatic nerve. Inadvertent trauma to these structures can result in pain and/or sensorineural deficits, which can be chronic in some cases.

Procedure Details

Safe and efficient BMH results from the consistent execution of many well-planned, clearly communicated steps. What follows is a detailed description of the procedure performed on a donor who has already undergone general anesthesia induction and intubation.

Patient Positioning—The intubated donor is pronated during transfer from the gurney onto the operating room table in careful coordination with the anesthesiologist, who controls the donor's head and neck and maintains the endotracheal tube. The shoulders are abducted to 90 degrees, the elbows flexed, and the forearms placed on arm boards in the “prone superman” position. Variation exists in operating table pads for pressure management, but key priorities include maintenance of a neutral neck position through the appropriate use of thoracic bolsters to elevate the torso and shoulders and placement of gel or foam pads under bony prominences, including the bilateral elbows, knees, shins, and feet. According to standard operating room practice, male genitalia must be positioned to avoid compression, and for female donors, the breasts must be positioned medially between the thoracic bolsters to avoid excessive pressure. To maximize exposure of the bilateral PSIS area, some harvesters elect to tilt the operating room table 10 to 15 degrees; this may be particularly useful for donors with thick subcutaneous tissue or prominent buttocks. Some centers make use of a Wilson frame, which provides easier access to the PSIS. Foam pads should be placed under the donor's arms to prevent external pressure from the frame on the brachial plexus.

Site Preparation—The bilateral PSIS are identified via surface anatomic landmarks and palpation. For hirsute donors, the lower back from the level of the superior margin of the gluteal cleft up to approximately L3 is depilated using electric clippers and/or adhesive mitts. An adhesive drape is applied to cover the buttocks, including the superior margin of the gluteal cleft, to prevent exposure of the mucous membranes and genitals to pooling of the antiseptic solution to be applied next. The skin is sterilized via scrubbing with an alcohol and chlorhexidine gluconate solution (or other suitable surgical skin prep) and left to dry for 3 minutes before the process is repeated. After the operators perform a surgical scrub and don sterile gowns, gloves, and eye protection, the site is draped with sterile towels and, where preferred, an adhesive antimicrobial incise drape. A sterile half sheet is placed over the donor's legs, followed by a fenestrated drape over the donor's cranial half, with the window exposing a wide operational site at the level of the iliac spines and crests.

Discussion with Anesthesia Staff—Before initiation of BMH, instructions specific to the procedure are reviewed with anesthesia staff. Please see Anesthesia section for additional details.

Operating Room Setup—The scrub table and Mayo stand are covered with sterile drapes and set up with the sterile equipment required for the harvest (delineated in Table A2). If using a pediatric scale to weigh the BM, it is covered with a sterile transparent drape and positioned where the harvest team will have unobstructed access.

Priming the Collection Bag—The BM collection bag is prepared by closing and securing any drainage ports. The BM collection bag is then primed with an anticoagulant solution. A reasonable practice would be to prime with 50 to 100 mL of a mixture of 20,000 units of heparin in 250 mL of lactated Ringer's solution, or 4000 to 8000 units of heparin. The priming volume can be approximated as 15 units of heparin per mL of final product multiplied by the lesser of the estimated BM volume required to achieve the TNC request or the maximum harvest volume for the donor. For example, a requested TNC of 80×10^8 cells with a reported average TNC concentration of 0.183×10^8 cells/mL would suggest a volume of just over 435 mL. A conservative minimum heparin concentration of 15 units/mL of final BM product would suggest priming with approximately 6500 units of heparin, or a volume of slightly over 80 mL. Given the importance of avoiding BM coagulation and in the interest of operational simplicity, it is common to round up the priming volume of heparin solution. The remainder of the anticoagulant solution is stored in beakers on the scrub table for priming collection syringes during the harvest.

Pediatric Scale—BM is more accurately quantitated by weight than by nominal volume according to the plastic collection bag. Therefore, when using a weight-based method for determining volume, a pediatric scale may be set up near the operating table and covered by a sterile clear plastic drape. The primed collection bag, along with any materials that will remain physically associated with it during the harvest (eg, Kelly clamps), is then weighed and documented, and the scale is tared before starting the harvest.

Mayo Stand—The Mayo stand is covered with a sterile drape and positioned over the donor's legs. The scrub nurse prepares six to eight 20-mL sterile Luer-Lok syringes by aspirating heparin solution from the beakers. The volume required is just enough to coat the inside of the syringe, in practice <0.5 mL. Primed syringes are placed on the Mayo stand along with BM needles and lap sponges.

Role of the Nursing Staff—The scrub nurse/technician performs several key activities during the harvest. First, the 20 mL syringes are to be primed with the anticoagulant solution. This requires just enough solution to coat the inside of the syringe, typically <0.5 mL. The scrub nurse should begin the case with 3 or 4 syringes per harvester so that there is always a primed syringe available on the Mayo stand, to allow the harvest to proceed efficiently. When the harvester places a syringe with BM back on the Mayo stand, the scrub nurse or laboratory technologist promptly transfers the BM into the collection bag at a moderate rate to minimize the time BM remains in the syringe, but not so forcefully as to cause excessive shear stress on the cells. The syringe is then reprimed with the anticoagulant solution and returned to the Mayo stand. The scrub nurse or technologist should intermittently massage the collection bag to ensure that the anti-coagulant solution and the BM remain well-mixed, visually monitor for the appearance of clots, and track the nominal BM volume. Clots in the collection bag should prompt consideration of more expeditious transfer of BM from the syringes to the bag and/or an increase in the priming volume of anticoagulant solution in the syringes. The harvesting team should discuss the provisional goal collection volume with the scrub nurse prior to beginning the case and instruct the scrub nurse to notify the team when they are approaching the halfway point.

Finally, the scrub nurse should be instructed to advise the harvest team when there is <50 mL of anticoagulant solution remaining, so that they can consider, based on how close they are to the provisional goal collection volume, whether to order an additional supply in time to avoid intraprocedural delays.

Open Collection System—An alternative to the above-described closed-system technique is an open system approach. Here an “open” collection bag is attached to a Fenwal BM collection stand and primed with a 10% isotonic solution of the predetermined collection volume at which a TNC cell count will be measured and 10 to 15 units per mL of heparin. Syringes for the proceduralists are primed as described above. The scrub nurse or procedure technologist empties syringes handed to them by the proceduralists through the open top into the collection bag. A typical approach is to perform a TNC count at a 600-mL collection volume. Therefore, the bag would be primed with 60 mL of Plasma-Lyte and 6000 to 9000 units of heparin. At the end of the 600 mL collection, some programs choose to add 10% of anticoagulant citrate dextrose (ACD-A) for additional anticoagulation, but others do not.

The content of the collection bag is then drained via 800- μ m, 500- μ m, and 200- μ m filters into the first product bag. The collection bag is then reprimed with isotonic solution and heparin in the same concentrations for the second part of the procedure. The volume of BM (and additives) for this part is determined through analysis of the TNC count gained from the midpoint sample, unless a program prefers to estimate the final collection volume through mathematical forecasting. At the end of the second collection part, ACD-A may be added, and the collected product is drained through the same sequence of filters into one or more product bags.

Harvesting Procedure—At many centers, BMH is performed by 2 operators, 1 positioned on each side of the prone donor. Following a standard preprocedural pause to confirm patient identity and intended procedural plans, the BMH begins with repalpation of the PSIS by the operator(s). The skin and soft tissue are held taut by the harvester’s nondominant hand, while the dominant hand is used to advance the BM needle with the stylet in place through the skin and subcutaneous tissue until the cortex of the iliac spine is contacted. Of note, BM needles of 11 gauge or smaller leave a sufficiently small skin defect such that the harvest site will heal well even without the use of an antecedent scalpel incision. With the needle tip safely below the skin, the harvester may stabilize the needle shaft with the nondominant hand while rotating the needle and applying downward axial force to penetrate the cortical bone.

Once the needle has entered the medullary space, which has a palpable gritty texture approximately 1 cm deep into the cortex, the BM is aspirated. This is done by removing the stylet and attaching an anticoagulant-primed 20- to 30-mL syringe to the trocar via the Luer-Lok mechanism. With the nondominant hand holding the trocar in place, the dominant hand withdraws the plunger. In an ideal pull, only modest force is needed to aspirate BM with a palpably heterogeneous texture. It should feel distinct from peripheral blood, which returns with minimal resistance and an almost velvety sensation. Sometimes bone spicules and fat globules are visible in the syringe.

When using a single-bevel trocar without barrel fenestrations, the needle is gradually rotated a full 360 degrees while aspirating to recover as much virgin BM as possible and to limit hemodilution. In theory, this is less impactful when using a fenestrated trocar, although there is little downside to needle rotation other than the minimal time required. Harvesters limit the volume of BM aspirated at a single depth and a single location to further mitigate hemodilution and maximize cell yield. Some limit the volume to 5 mL per pull, whereas others take as much 20 mL per pull. This practice is influenced by data showing higher TNC concentrations with smaller-volume pulls, although the impacts of smaller-volume versus larger-volume pulls on final cell yields and on patient outcomes remain to be determined. Larger-volume pulls are more common when using multi-fenestrated trocars. The BM-filled syringe is disengaged from the BM trocar and placed on the Mayo stand for the scrub nurse to transfer into the collection bag.

Two well-accepted methods of aspirating BM have been established. One method involves limiting aspirations to 5 mL per pull, to minimize hemodilution. After each pull, the stylet is replaced and the needle with stylet is removed, before entering a separate area of the cortex (through the same skin puncture site). Ultimately, 2 or 3 skin puncture sites over each iliac crest are sufficient to achieve the desired BM volume. Another method involves replacement of the stylet after aspiration and allows up to 20 mL per pull, followed by advancing the needle 3 to mm 4 deeper into the medullary space while rotating the needle back and forth. The stylet is removed, and another aspiration is performed in the same manner as the first. The stylet is replaced, and the entire needle is removed from the iliac bone and the deep subcutaneous tissue, but not from the skin. The needle is then redirected by several millimeters to identify an unperturbed area of the iliac spine. The process of BM aspiration in this new site is then performed as was done at the previous site. By gradually marching along the iliac spines in this manner, the harvesting team can collect at least 1 L of BM from the PSIS through 2 or 3 skin puncture sites on each side in most donors, even when limiting aspirations to smaller volumes with each pull.

If additional BM is needed to achieve the requested volume or TNC count at the point when fresh sites on the iliac spines accessible through the initial skin puncture site have been exhausted, palpation can identify a site 5 to 7 cm superior and lateral along the iliac crest for a second skin puncture on each side. The iliac crest is narrower than the iliac spine, but a reasonable expectation would be to recover an additional 500 mL of BM from the additional 2 skin punctures (1 on each side). In some cases, it may be necessary to pursue a third skin puncture site on each side, another 5 to 7 cm superior and lateral along the iliac crest, although the yield typically diminishes with tertiary sites.

Cell Count Measurements—A white blood count (WBC) or TNC is sent off the collected BM at 1 or 2 points during the harvest, once near the halfway point and then at the end. A reasonable strategy is to consider the halfway point when one-half of the goal volume has been obtained (when the request is denominated in volume) or when one-half of the estimated goal TNC volume has been collected (when the request is denominated in TNC). A convenient approach for the latter scenario is to divide the requested TNC by the average BM nucleated cell concentration (0.183×10^8 cells/mL). For example, a requested TNC of 175×10^8 would imply a provisional goal volume of just over 956 mL and a

halfway point of approximately 475 mL of collected BM. At the halfway point, 3 mL of BM is withdrawn from the collection bag using a sterile 10-mL syringe and sent for WBC/TNC analysis. It is advisable to err on the side of checking early, given that the time required to obtain the BM WBC results limits the actionable window for this information.

With the BM WBC results, the goal collection volume can be estimated more precisely by dividing the requested TNC by the WBC count from the BM. Although the BM at the halfway point is diluted by the anticoagulant solution used to prime the collection bag, the provisional goal volume calculated in this manner remains a reasonable estimate because of hemodilution later in the harvest, additional anticoagulants that may be added at the end of the case, and cells lost during product filtration. A prudent strategy is to collect approximately 10% more than the provisional goal volume, as permitted by the donor's weight-based maximum harvest volume, to accommodate the TNC dilution that can be expected with increasing collection volume.

Once this adjusted goal volume has been collected, additional heparin is added to the product to achieve a final concentration of 15 to 20 units/mL. Some transplant physicians request the addition of ACD-A to the BM product, generally at a final ratio of 1:10 by volume. An additional WBC count is obtained to estimate the cell counts coming from the operating room, as well aerobic and anaerobic cultures for sterility testing.

Assessing Progress—The impact of the stem cell dose on engraftment outcomes mandates using the most accurate method to monitor progress during BMH. The markings on BM collection bags constructed of polyvinyl chloride or similar flexible, transparent plastic material are inaccurate owing to heterogeneity in bag shape and expansion properties. The nominal bag volume increases nonlinearly with the addition of BM. A more accurate method for monitoring collection progress is by BM weight; however, not all programs use this method. Weight-based methods use the specific gravity of BM, which has been empirically measured as 1.058 g/mL. By measuring the weight of the primed collection bag and taring the scale prior to BMH (see Pediatric Scale above), subsequent measurements will reflect the weight of the collected BM. Dividing this weight by the BM specific gravity provides an accurate volume of collected BM. Multiplying this calculated BM volume by the WBC count of the BM at the halfway point will provide the most accurate estimate of the current TNC count. Another way of using this information is to divide the requested TNC count by the WBC count of the BM and then multiply the result by the BM specific gravity; this provides the goal BM weight against which the harvest team can assess progress (Figure 3).

Concluding Actions—The BMH procedure is completed finished when one of the following occurs: the final cell dose is attained, the maximum volume is collected, or the maximum time of anesthesia is reached. On reaching the adjusted goal collection volume, adding additional heparin and other requested anticoagulant solution, and sending the end of harvest specimen for TNC and other requested cell counts and microbiologic testing (see Cell Count Measurements above), the harvester passes the BM through inline 200- μ m and 500- μ m filters en route to one or more final collection bags. Typically, if a product will be processed on site, a single large final collection bag is used, whereas a product that will be

shipped via courier is transferred to 2 or more bags to minimize the risk of bag rupture or leakage during transportation. In either case, air is removed from the head space of any filled collection bags before securing the product via clamping and tying the tube with a double knot. Product labels provided by the donor coordinator are then affixed to the final collection bags, and the labeled collection bags are handed off to the donor coordinator for transport to the cell manipulation laboratory or the courier.

In CCs that use local analgesia after BM collection, a member of the team administers the local analgesia to the harvest site using a spinal needle at least 3.8 cm long, longer as needed for donors with thick subcutaneous tissue. The analgesic is administered to all areas of the periosteum perturbed by the harvest. One reasonable option is the application of 0.25% bupivacaine without epinephrine, 10 to 15 mL per side. This would correspond to a total bupivacaine dose of 50 to 75 mg, well below the maximum recommended local infiltration dose of 175 mg. Using a larger-gauge needle (18 to 21 gauge) may be helpful, given that saturating the periosteum requires significant redirection of the needle, and a larger-gauge needle will better maintain its intended direction rather than following previous soft tissue tracts. After administration of local analgesia, firm direct pressure is provided over all skin puncture sites for a minimum of 5 uninterrupted minutes to achieve complete hemostasis.

Surgical drapes are then removed, including the adhesive antimicrobial incise drape (if used), and the skin is gently cleansed with water or saline solution to remove any blood. A pressure dressing is then applied. An example of such a dressing would be the placement of 2 ABD pads over each PSIS/PSIC area, topped by generous fluffed or rolled gauze and secured in place by Microfoam or Elastoplast surgical tape. The donor is flipped back into the supine position and when available placed onto abdominal binders (as many as required to cover the harvest site fully), which are used to augment the pressure dressing during the immediate postharvest period. The donor is then extubated and returned to the postprocedure recovery unit.

Troubleshooting

This section examines some common and/or significant challenges that arise during BMHs and proposes strategies for addressing them.

Large Donor Body Habitus—Thick subcutaneous tissue exceeding 5 cm, as in some obese donors, poses several challenges to the harvesting physician. First, it often requires the harvester to direct the axial force of the needle over a greater distance to the tip. Even attempts to stabilize the needle with the nondominant hand are more difficult, because the thicker, soft tissue creates a longer distance from the point of bone contact. Second, a higher body weight is associated with greater bone density, and maintaining a consistent axial direction when applying greater force requires considerable dexterity. Third, obese donors have larger weight-based maximum harvest volumes, compounding both of the afore-mentioned challenges. Additionally, passing the needle through more soft tissue increases the opportunity for vascular trauma and bleeding, which is more difficult to detect and control given the obscuring and cushioning effect of soft tissue.

Several strategies may help address these challenges. When positioning the donor, consider tilting the operating table 10 to 15 degrees at the level of the pelvis. This will marginally extend the soft tissue overlying the PSIS/PSIC area and facilitate keeping the tissue more taut, which will enhance control of the harvest needle. A longer harvest needle (up to 15 cm) may be needed to access the medullary space of the iliac bone safely. It will be necessary to stabilize the trocar with the nondominant hand once the tip has penetrated the skin to improve directional control. If accessing the medullary space proves very challenging and/or inefficient, it would be reasonable to compensate by aspirating a larger volume of BM with each pull and aspirating from more than 2 depths. The resulting hemodilution must be weighed against the alternative, which would entail fewer total aspirations or a longer duration of general anesthesia, neither of which is ideal. Finally, it is essential that the harvest team maintains firm, uninterrupted manual pressure over the harvest sites for at least 10 minutes and repeat this as necessary to ensure the complete cessation of postprocedure oozing before applying the harvest site dressings.

Dry Taps—Most dry taps are intermittent events that can be rectified by adjusting the depth of the needle or repositioning the needle altogether. Sometimes repeated dry taps result from harvest saturation of regions of the PSIS/PSIC area toward the end of a longer case. In these cases, the skin, soft tissue, and cortical bone no longer maintain a seal with the trocar, such that pulling back on the barrel of the syringe aspirates ambient air instead of BM. Pinching the skin around the trocar entry site with the fingers of the nondominant hand to restore a seal can salvage some of these aspirations but is at best a short-term remedy. This is a sign that a new harvest site is needed, which may require a secondary or tertiary skin puncture to locate untapped bone. In rare instances, repeated dry taps are encountered at the outset of a harvest. Some of these occurrences may be related to anatomic variation and oblique engagement of the BM needle with the iliac cortex, resulting in longer passages of the needle through cortical bone without entrance into the medullary space. This problem can be addressed by angling the BM needle 10 to 15 degrees medially to engage the iliac cortex more perpendicularly and thereby reduce the required depth of cortical penetration.

Dense Bones—Harvesting BM through dense bones can become physically taxing, particularly with larger-volume harvests. Maximizing mechanical efficiency through the use of proper ergonomic technique and equipment is a critical priority. The harvester should first optimize the use of gravity by placing himself or herself above the operative site through a combination of lowering the table height and standing on one or more surgical step stools. When penetrating the cortical bone with the harvest needle, the harvester should position his or her shoulder directly above the iliac bone, such that physical force is applied in a straight line from the shoulder through the arm and the harvest needle into the cortical bone. The larger, stronger muscle groups of the shoulder girdle are thereby engaged. (Note that the harvester is not passively leaning on the needle, which would be hazardous.) This not only will improve the efficiency and safety of cortical bone penetration by focusing the axis of force, but also will minimize the risk of overuse injury to the harvester's shoulder. Of course, when greater physical forces are applied, it is important to stabilize the barrel of the trocar with the nondominant hand to reduce the risk of needle slippage and resulting tissue trauma.

Two other issues that become more prominent with dense donor bones are stylet lodgment in the trocar and dulling of the stylet. The former can result from deformation of the trocar, whereas the latter results from materials fatigue at the stylet tip. If the stylet cannot be manually withdrawn from the trocar, it may be necessary to use an extra Kelly clamp to do so. When this occurs, the harvester should replace the entire needle apparatus (trocar and stylet) with a new one. To mitigate this risk and to address the issue of stylet dulling, it is prudent to replace the stylet as soon as the efficiency of cortical penetration appears to decline.

POSTPROCEDURE DONOR ASSESSMENT

Following BMH, most donors are not admitted for overnight observation; however, several centers have a routine overnight hospital admission policy. In a study of 2726 unrelated volunteer NMDP BM donors, one-third of donors were hospitalized overnight; however, the majority were admitted in accordance with routine practice, and only 1% required 2 or more nights because of complications [15]. Overnight hospital admission is strongly recommended in cases where no donor caregiver is available on the day/evening of the BMH. If discharge on the day of collection is anticipated, the donor should be told what criteria need to be met before discharge from the recovery room to the charge of their caregiver. Criteria for safe discharge to discuss should include the following:

- Pain control. The donor's pain needs to be adequately controlled on oral pain medication and the donor should have appropriate analgesia for discharge.
- Nausea control. The donor should be without severe nausea or vomiting such that they will be able to manage oral analgesia after discharge and be given anti-nausea medications on discharge if required.
- Micturition. Ensure that the donor can pass urine prior to discharge. If a donor has not passed urine, a bladder scan should be performed to confirm urinary retention. A fluid challenge may be attempted if there is a low volume urine in the bladder, but then intermittent or full catheterization may be required to ensure comfort. If retention persists, the donor may need to be admitted overnight.
- Stable blood pressure. Orthostatic hypotension is not an uncommon complication following the procedure and often can be avoided by ensuring adequate fluid replacement during and after the harvest. If orthostasis is persistent despite adequate hydration, another etiology should be considered, including anesthesia, antisickness, or pain medication. The donor may need overnight admission and alternative pain medication.
- Suitable caregiver. As stated above, if a suitable caregiver is not available to accompany the donor overnight, this may be an indication to admit for observation.
- Assessment of postprocedure CBC/Hct/Hb. This will allow confirmation of the anticipated Hct or detect any unexpected drop in Hct with the determination of the need for blood transfusion or for further investigation of blood loss prior to discharge. Often in centers where the donor is followed up on the

day after procedure, the donor may have only a repeat Hct the next morning. Recommendations would be in large-volume collections that a Hct be completed prior to discharge; however, caution is needed to avoid potential hemodilution of the sample.

At the time of discharge, the CC should ensure that the donor has been provided with postdonation care instructions with contact names and phone numbers.

Recommendation:

If the donor meets the clinical criteria for discharge on the same day of the BMH, the donor should be discharged with a caregiver. If the donor does not have a care-giver available on the day of procedure consideration should be made for admitting the donor for observation overnight.

DONOR FOLLOW-UP

As described above, a dressing is applied to the skin puncture sites at the time of completion of the harvest, and the donor (and caregiver) should be instructed (with written instructions if available) on how to physically care for the wounds and when to seek medical attention. In most cases, the dressing can be removed after 24 hours and the wounds reviewed by the donor and/or caregiver. The donor should avoid full submersion in water, such as bathing or swimming, until the wounds are closed; showering is acceptable.

The local application of ice packs to reduce swelling and inflammation postharvest is recommended, and if possible, started early postprocedure while the donor is in the recovery area. Ice packs can even be applied above or below the dressing to aid vasoconstriction. After several days, once the acute swelling has subsided and the wound site is no longer oozing, use of a heat pack may be appropriate, especially in larger-volume harvests after which a sizeable hematoma may have developed.

Pain control may require the use of opiates/narcotics either alone or in combination with acetaminophen for at least the first 2 or 3 days after BMH, especially following large-volume collections. In combination with ice and heat packs, as suggested above, pain may then be reasonably well controlled with acetaminophen alone. The peak of discomfort after BMH occurs within 48 hours of the procedure; 60% of donors may continue to report pain at 1 week postharvest, and 90% report full recovery at 8 weeks [15]. Donors should avoid nonsteroidal anti-inflammatory medications, including aspirin, naproxen, and ibuprofen, for at least 1 week and until all wounds are healed and oozing has ceased.

Donors should be advised to avoid high impact exercise or strenuous activity for 10 to 14 days after the procedure. This will allow full healing of the subcutaneous tissues and, in particular, torn muscle fibers. The donor ideally should not lift objects weighing more than 10 pounds during this time to prevent the risk of chronic pain. Normal walking is beneficial to prevent stiffness and should be recommended.

Supplemental iron should be considered to aid recovery of Hg concentration in large-volume BMH and hypoferritinemic donors. A prescription may be provided at the time of the preharvest review/consent or earlier, and the supplemental iron can be started before BMH and continued for 1 month after the procedure.

Follow-up with either the donor center or the CC should be provided according to local center or NMDP guidance. The donor and/or caregiver should alert the donor center or their respective NMDP contact of any increasing redness, pain, discharge, fever, and other signs of potential infection or other complications.

The median time to complete recovery for donors who fully recovered was 2.3 weeks in the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) phase III randomized multicenter trial 0201 [37]. Other studies have suggested between 10 days and 3 weeks [13,16]. A flowchart of the entire process from preharvest donor review to the BMH and finally postprocedure donor assessment is shown in Figure 4.

CONCLUSION

The process of BM donation to provide a stem cell product for a related or unrelated recipient with a significant malignant or nonmalignant hematologic condition not only is associated with physical adverse effects, but also may be associated with some psychological burden [8,38]. The process of donation is an incredibly altruistic gift from the donor, who often becomes heavily emotionally invested in the outcome of the recipient. At the time of the consent process as well as at discharge, the donor is a true hero to the intended recipient of their BM. Regardless of the outcome of the planned transplantation procedure, the donor ultimately has done everything they can to help save the life of that person.

This white paper describes the BMH process in detail to ensure that providers who perform BMH provide patients with the optimal stem cell products while achieving donor safety. All authors have contributed to the preparation of this paper and acknowledge the nuances and small variations among CCs. This guideline serves as a recommendation that may help centers refine their practice and ensure that donor safety remains paramount while providing recipient with quality products.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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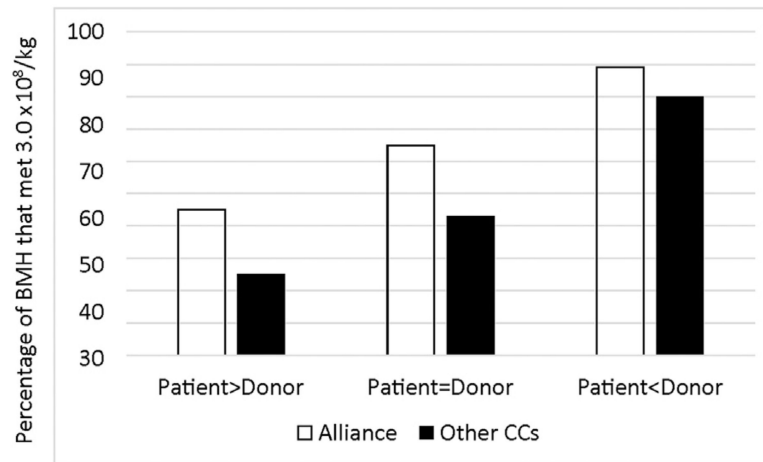


Figure 1.

Percentage of BMHs that met the target cell dose of $3.0 \times 10^8/\text{kg}$ cells from the Alliance CCs and the other CCs based on the difference in donor and recipient weight. > indicates that the recipient weighs at least 10 kg more than the donor. = indicates that the recipient weight and donor weight are within 10 kg of each other. < indicates that the donor weighs at least 10 kg more than the recipient.

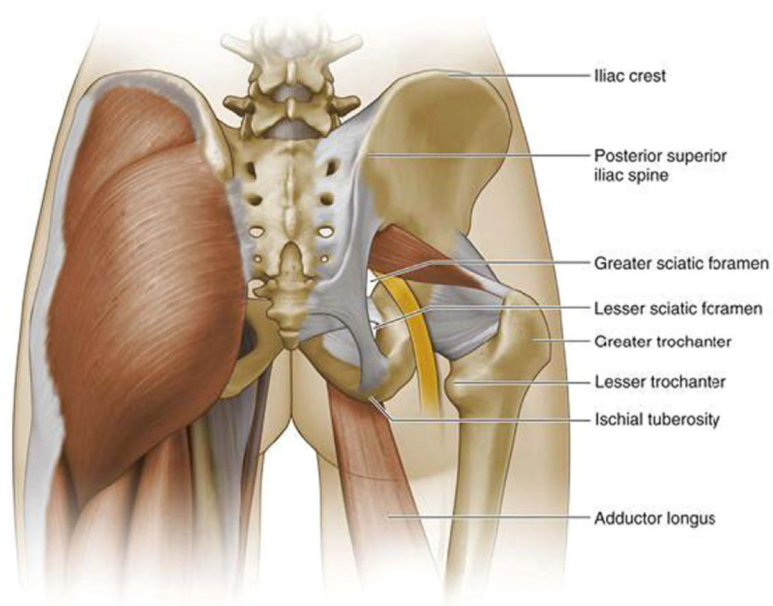


Figure 2.
Posterior iliac anatomy guides site selection for safe and efficient BMH [39].

$$\text{Goal BM weight (g)} = \frac{(\text{requested TNC count}) \times 1.058 \text{ g}}{(\text{BM WBC count}) \quad \text{mL}}$$

Figure 3.
Formula for estimating BM goal weight against which to assess collection progress.

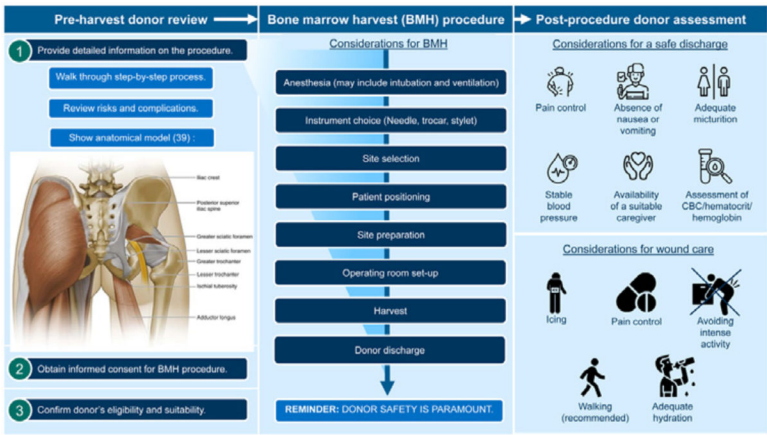


Figure 4. Flowchart of the entire BMH process from preharvest donor review to the BMH and finally postprocedure donor assessment [39].

Table 1

Median TNC Dose from BMH at Alliance CC and Other CCs

Recipient Weight, kg	Median TNC Dose, $\times 10^8/\text{kg}$	
	Alliance CCs	Other CCs
≤ 30	8.3	7
>30–40	5.7	5.3
>40–50	4.8	4.1
>50–60	4.3	3.2
>60–70	4.4	3.5
>70–80	2.7	2.6
>80–90	3.4	2.1
>90–100	2.5	2.2
>100	2.1	1.9

Table 2

Complications of BMH

Complications	Description
Common complications (occurring in 20%–85% of BMHs)	BMH site pain, back pain (mechanical), fatigue, nausea, vomiting, sore throat, headache, pain at i.v. site)
Less common complications (occurring in <20% of BMHs)	Fever, bleeding, large hematomas, minor wound infections, hypotension, urinary retention, syncope, chipped teeth
Serious complications (occurring in 1% of BMHs)	Deep infections, abscesses, bacteremia, prolonged pain, sacroiliitis, numbness, neuropathy, prolonged hospitalization, seizure
Life-threatening complications (rare)	Myocardial infarction, severe pain, anaphylaxis, prolonged paralysis after anesthesia, pulmonary embolism, fat embolism, blood transfusion complication, malignant hyperthermia, pulmonary edema, arrhythmia, stroke, death

Table 3

Example of Calculation for Anticipated Blood Loss and Post-BMH Hct

Donor weight and sex: 60 kg female
Estimated total blood volume: 60×70 (or $\times 75$ for male) = 4200 mL
Donor's preharvest Hct: 35%
Baseline total RBC volume: $4200 \times .35 = 1470$ mL
BMH volume: 800 mL RBC content in BM product: $800 \times .30$ (ie, assume BM 30% Hct) = 240 mL
Estimated soft tissue RBC loss: $300 \text{ mL} \times .35$ (ie, 35% Hct) = 105 mL; total RBC loss: $240 + 105 = 345$ mL
Estimated post-BMH Hct: $1470 - 345 = 1125$ mL; $1125/4200 = 27\%$

Table 4

Timing of Communication with Anesthesia during BMH

Timing	Options
Before BMH	Discuss the estimated BM volume to be collected.
	Request a second i.v. line and discuss the targeted replacement volume and possible speed of fluid replacement therapy.
	Remind the anesthesia team to not administer corticosteroid drugs until the collection has been completed.
	Discuss the options for postoperative pain management, which may include a preoperative dose of acetaminophen but should not include any nonsteroidal anti-inflammatory drugs (eg, Ketorolac), to avoid postoperative bleeding.
	Indicate that intraoperative antibiotic drugs are not required.
During BMH	Provide updates on harvest volume collected.
	Inquire about status of fluid replacement and donor vital signs.
End of BMH	Report the total BM volume collected to the anesthesia team.
	Inquire about fluid replacement management and record replacement volumes in procedure notes.
	Indicate that corticosteroids may be given at this time to treat or prevent postanesthesia nausea.
	Remind the anesthesia team that nonsteroidal anti-inflammatory drugs should be avoided for the first 72 hours post procedure.

Table 5

BMH Needle Comparison According to Selected Features for Adult Donors

Feature	Options	Pros	Cons	Recommendation
Needle length	6–8 cm	High degree of control even with dense bones	Limited depth of penetration	~10 cm in most circumstances A longer needle may be useful with >5 cm subcutaneous tissue.
	9–11 cm	Good control and adequate depth of penetration for most donors	May become hubbed with very thick subcutaneous tissue	
	13–17 cm	Greater penetration through subcutaneous tissue	Less control, particularly with dense bones	
Trocar size	8–9 gauge	Rapid aspiration, low shear stress on cells	Slightly more traumatic	11 gauge in most circumstances
	11 gauge	Efficient aspiration, low shear stress on cells	Marginally more difficult to penetrate dense bones	
	13–15 gauge	Potentially easier to penetrate dense bones	Slower aspiration or greater shear stress	
Trocar tip beveling	Single	Greater area for aspiration through tip with acute bevel angle and oblique orifice	Need to rotate needle during aspiration	Single bevel (marginal advantage blunted by barrel fenestrations)
	Multiple	Theoretically more effective for coring (less relevant with stylet in place)	Smaller area through which to aspirate (though less relevant with barrel fenestrations)	
Trocar barrel fenestrations	Yes	Simultaneous aspiration from multiple depths and directions may mitigate hemodilution; obviates needle rotation during aspiration		Fenestrated barrel (marginal advantage blunted by oblique angle bevel at tip)
	No		Aspiration through a single point may necessitate smaller pulls to minimize hemodilution Need to rotate needle during aspiration	
Stylet handle	Recessed	Very clear whether stylet has been fully advanced within trocar barrel	Withdrawing stylet from trocar may require concentrated manual force through fingertips, which may cause finger fatigue and discomfort	Twist lock (*operator preference)
	Twist lock	Provides tactile feedback for proper stylet position within trocar barrel Greater contact area with fingers when withdrawing stylet from trocar can be more comfortable		
Stylet tip	Pyramidal tip	Allows for focused application of force while engaging cortex		Pyramidal tip stylet