

113

THE "MARROW-MINER": EFFICACY OF A NOVEL, MINIMALLY INVASIVE BONE MARROW HARVESTING DEVICE IN PRE-CLINICAL EVALUATION & FIRST HUMAN EXPERIENCE

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Introduction: Bone marrow (BM) contains a rich supply of adult stem and progenitor cells, and may have long-term advantages over PBSC for many allo-transplants. Traditional percutaneous large bore needle aspiration methods for harvesting marrow are crude, tedious and expensive and usually require general anesthesia. A novel device, the MarrowMiner (MM) was developed for the minimally invasive harvest of BM to enable the rapid, convenient, outpatient harvest of large quantities of BM under local anesthesia for use in BMT and an increasing array of regenerative therapies. The MM has been tested extensively in human cadavers, in large animals, & following recent FDA 510(k) approval, in initial human subjects. **Methods:** In 5 juvenile pigs, standard 1 and 6-port needles were used to aspirate marrow along the left iliac crest. On the right iliac, the MM device was used to collect BM. Harvests were collected in: small (5 ml), medium (6–20 ml), & large (>20 ml) volumes. BM viability, cell counts & CFU-F assays were performed. Initial human subjects similarly had traditional needle harvests performed, followed by MM harvest on their opposite hip. **Results:** In the porcine study the MM was observed to be safe, with the catheter remaining within the marrow cavity in up to 20 cm long passes. >60 ml of marrow could be aspirated in a single pass. BM aspirated along the iliac crest by the MM contained a significantly higher concentration of nucleated cells and CFU/ml than by standard needles. As expected, the CFU concentration decreased with increasing volume aspirated by standard needles while no CFU dilution occurred with the MM. The MM yielded significantly higher CFU/ml than the standard needles with medium and large volume aspirates, where the MM harvested 9 fold more CFU-F/ml than the 6-port needle (table). In initial human subject experience, the MM was safe, effectively collected BM, with no post-procedure pain or complications, and higher CD34+ counts compared to needle aspirates. **Conclusions:** In a porcine model, the MM can successfully & safely harvest large volumes of BM, with significantly higher stem cell content than traditional needle aspiration. The flexible shaft allowed for aspirating BM of the highest cellularity along the iliac crest, a path unfeasible for rigid needles. These results, as well as initial, ongoing clinical studies suggest that this novel MM device may enable significantly improved BM harvest in a more rapid, reproducible & less invasive manner.

CFU/ml Content of Marrow from Traditional Harvest Aspirates and from MarrowMiner

Aspirate Size	1 hole needle	6 hole needle	MarrowMiner (MM)
Small Volume	1111	ND	ND
Medium Volume	516	1690	2623
Large Volume	ND	226	2335
Along Iliac Crest	NA	NA	5313

Mean CFU-F/ml (five, 65–75kg juvenile pigs).

114

THE RATIO OF COLONY FORMING UNIT (CFU) TO TOTAL NUCLEATED CELL (TNC) COUNT PREDICTS ENGRAFTMENT IN UMBILICAL CORD BLOOD TRANSPLANT

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Umbilical cord blood (UCB) is increasingly utilized as a graft source for hematopoietic cell transplant; however, both graft failure and delayed engraftment remain significant obstacles to successful

UCB transplantation. Graft characteristics correlated with improved engraftment and survival include total nucleated cell dose (TNC), degree of HLA match, CD34+ cell dose, and colony-forming unit assays (CFU). While TNC has been considered the most consistent predictor of engraftment and survival, analysis of the relative contribution of these variables is complicated by the strong correlation between TNC, CD34+, and CFU doses. We hypothesize that the ratio of CFU to TNC is a cell dose-independent measure of graft hematopoietic potential that may be prognostically useful in future graft selection algorithms.

The Saint Louis Cord Blood Bank has been performing CFU assays on all UCB units since 1996. Since 2002 the CFU/TNC ratio has been utilized in our storage eligibility algorithm, with units having <2 colonies/10⁴ nucleated cells considered ineligible for banking. Engraftment data was analyzed for 237 acute leukemia patients >10 kg who received a single UCB transplant after myeloablative conditioning, and grouped into quartiles according to post-processing CFU/TNC ratio. Patients without evidence of engraftment were censored at day 60.

Median time to neutrophil engraftment (ANC > 500) became shorter with each advancement in quartile (Table 1), and was 7 days faster in the highest CFU/TNC quartile compared to the lowest (p = 0.0007). A similar trend was seen in 66 patients with post-thaw CFU data available. There was no difference in TNC dose, degree of HLA match, or patient age amongst the four quartile groups. CD34+ cell dose was greater in the highest CFU/TNC quartile compared to the lowest (P < 0.05).

Several authors have shown a relationship between higher CFU dose and faster engraftment. However, higher CFU dose is correlated with higher TNC dose. This, in addition to inherent variability in CFU testing, has led to the use of TNC dose but not CFU dose for determining the best graft for use in UCB transplant. We show that CFU/TNC ratio can be a powerful independent predictor of rapid engraftment. Further study will be required to determine if this parameter will allow identification of grafts with relatively small cell doses that might still have the potential for successful engraftment.

Table 1. Time to Neutrophil engraftment by CFU/TNC ratio

Post Processing Ratio Group	n	Median Time to ANC > 500 (days)
<6.0/10 ⁴	57	26
6.0–7.7/10 ⁴	58	24
7.7–9.3/10 ⁴	62	21
>9.3/10 ⁴	57	19

115

COST EFFECTIVENESS OF COLLECTION STRATEGIES FOR CD34+ PROGENITOR CELL DETERMINATIONS IN AUTOLOGOUS HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION

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Background: Peripheral CD34 counts can optimize timing for collection of adult mobilized hematopoietic progenitor cell (HPC) products for transplantation to treat hematological malignancies. The ability to accurately predict a successful CD34 collection can reduce the number of multiple low-CD34+ collections, easing the burden of collection for the patient and the collection and processing facilities. Our hypothesis is that increasing the circulating CD34+ threshold will result in a cost savings over strategies of no threshold and the current threshold of 4 CD34+ cells/μl, while resulting in a greater proportion of successful collections. **Methods:** A decision tree was programmed in TreeAge Pro Suite 2006 v1.3 (TreeAge Software, Williamstown, MA) and a cost analysis run comparing "no threshold" to varying thresholds. Probabilities were determined from a dataset