The OsteoAccess System – Low-Force, Controlled Angled Bone Access for Bone Biopsy and Bone Marrow Aspiration a NIH/NCI SBIR Funded Platform

M.L. Mulvihill[*], E.D. Ashuckian[*], J.K. Greaser,[*] H. Hartung[**], M.D., K.M. Erdley[*] and R.B. Bagwell[*]
*Actuated Medical, Inc., Bellefonte, PA, 16823.
**Children's Hospital of Philadelphia, Philadelphia, PA 19104

ABSTRACT

For diagnostics procedures following bone lesion identification as well as other medical causes, bone marrow biopsies are often required. Current methods to perform bone biopsies require significant forces to penetrate cortical bone, are unable to perform insertions at low inclination angles (<50°), and often require additional samples (and bone insertions) due to inadequate initial sampling. These combined factors can lead to extended procedure time, which in turn can increase radiographic exposure and in pediatric cases, time under anesthesia to patients. The OsteoAccess System is a patented novel medical advancement that allows clinicians greater flexibility in planning the path to the lesion by enabling oblique angle penetration, providing easier anchoring into bone surfaces with high curvature, and allowing greater control by reducing penetration force. These system attributes will significantly benefit bone lesion biopsy outcomes, improving overall safety and sample quality. Actuated Medical, Inc. (Bellefonte, PA) is developing the OsteoAccess System using a National Institutes of Health / National Cancer Institute (NIH/NCI) Small Business Innovation Research (SBIR) Phase II grant.

Keywords: bone biopsy, cancer, hematology, intraosseous infusion, bone marrow

BACKGROUND

Various medical and diagnostic procedures require penetrating hard cortical bone to perform percutaneous bone marrow biopsies. Bone lesions identified through imaging or clinical evaluation are biopsied to obtain the required tissue to diagnose a wide range of potential cancers and blood diseases. Sampling locations can include the iliac crest (hips), legs, arms, spine, or ribs. It is estimated that >50,000 bone lesion biopsies are performed on patients, and >25,000 patients are diagnosed with a malignant bone tumor annually in the USA [1]. The OsteoAccess System (see **Figure 1**) is an innovative bone access device that reduces insertion force, improves clinician control, and provides more favorable paths for entry into the target.

Currently, the most common method of performing bone marrow biopsies is using a Jamshidi® needle consisting of an 11 gauge cannula surrounding a 15 gauge trocar-tipped stylet attached to a "T" shaped handle. To penetrate through cortical bone, the trocar tip is twisted and ground with high force against the bone until the outer cannula is worked completely through the cortical layer. The stylet is then removed, and bone marrow is aspirated through a syringe attached to the cannula via a Luer-lock connection. Additionally, a core sample is obtained by twisting the cannula into the cancellous bone.

Figure 1: The OsteoAccess System enables angled bone access.

The design of Jamshidi-style needles falls short of addressing many challenging aspects of biopsy procedures. It cannot obtain samples at low inclination angles (<50°), and the significant forces (see **Figure 2**) required to penetrate the cortical bone limits the operator's fine control. Under such excessive forces, the risk to surrounding tissue when attempting to penetrate obliquely or on irregular or highly curved cortical surfaces severely limits the ability to safely sample from ribs, vertebrae and other bones adjacent to delicate or vital structures. For adult patients, bone lesion biopsies are often performed under CT-image guidance to ensure accurate sampling [2, 3]. However, the gantry prohibits the clinician from generating enough leverage on the biopsy system. This often requires pulling the patient out of the imaging gantry to improve leverage, and advancing the device "blindly". The patient is then pushed back in to re-check positioning, and the process is iterated, adding to procedure time [4].

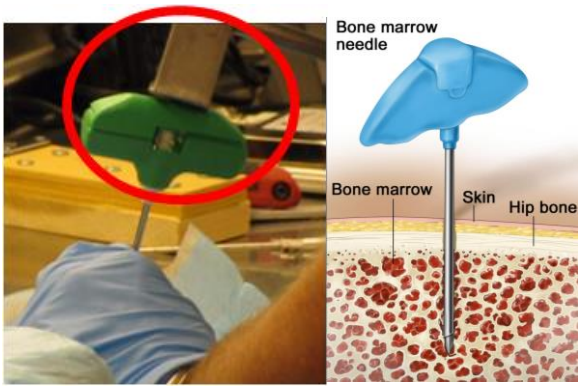

Figure 2: With traditional bone biopsy, a mallet is often required to force the biopsy needle through cortical bone, gaining access to the bone marrow [8].

Because high forces pose challenges for precise, controlled insertions, core sample quality ultimately suffers. Samples of inadequate length, too much cortical tissue, or artifacts due to rotation, rocking and compression-decompression must be repeated [5] (see **Figure 3**). This leads to clinician fatigue and increased patient discomfort, anxiety, and healing time [6, 7]. The recommended biopsy core length for the most accurate diagnoses is 1.5 - 2 cm [9, 10]; however, a study focusing on pediatrics concluded that 17% of the submitted 822 bone marrow specimens examined were inadequate [11]. Additionally, of the 13 centers submitting at least 20 core samples, failure rates ranged from 2.6 to 50% [11]. A similar study considered 25% of 605 pediatric bone marrow biopsies examined inadequate [12].

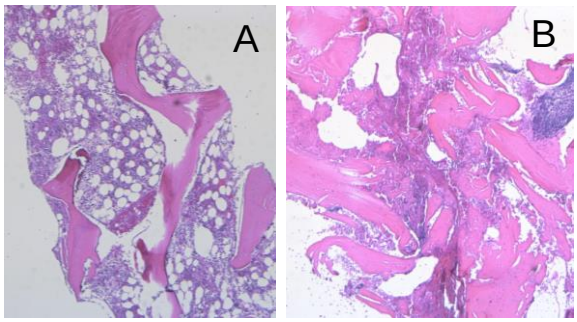

Figure 3: Examples of A) Adequate bone marrow specimen and B) Sample with crushed artifacts and hemorrhage.

Re-seeding of tumor cells along the biopsy needle track, leading to cancer recurrence, is a recognized risk with primary sarcomas [13, 14]. Recurrence of bone tumors is particularly lethal, with 5-year survival rates as low as 14% [15, 16]. If tumor resection is required, the entire biopsy needle tract must also be removed along with portions of transected tissue compartments [2]. In order to ensure the best prognosis and the option of limb-sparing resection, the clinical team must carefully plan out the approach to the lesion to ensure the needle track avoids vital structures and tissue compartments while obtaining the highest quality biopsy sample possible [2, 17]. Biopsy paths that are poorly planned or limited by anatomical location can lead to functional limb loss or even unnecessary amputation (5-8% of cases) [18]. The range of possible paths is partially limited by current technology and its inability to penetrate the cortical bone at low inclination angles and the high forces that limit control.

THE SOLUTION

A device that allows greater flexibility in planning the path to the lesion by enabling oblique angle penetration, and easier anchoring into bone surfaces with high curvature, while at the same time allowing greater control by reduced penetration force, would significantly benefit bone lesion biopsy outcomes, improving overall safety and sample quality. The OsteoAccess System's patented [19-21] technology oscillates a needle system under precise electronic control to enable low-force, angled penetration of rounded, hard surfaces where traditional needles and drill bits tend to slip dangerously off the surface. This actuation would significantly reduce the above discussed risks and repeat procedures.

BENCHTOP DATA

Benchtop testing of the OsteoAccess System demonstrated its ability to reduce the insertion force required to enter a cortical and cancellous bone. Insertions were performed to a depth of 10 mm with a solid 11 gauge needle in 37°C hydrated porcine hock bones. Insertion force was measured

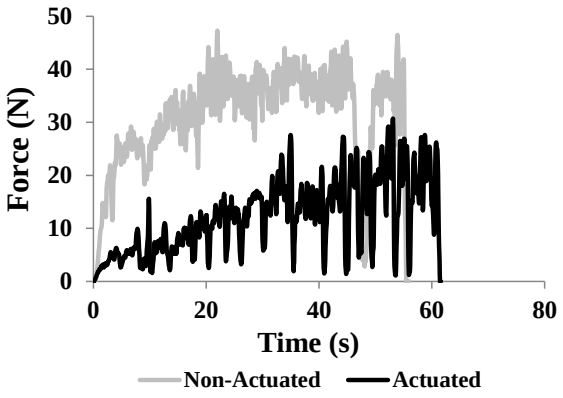

Figure 4: Force profiles during non-actuated and actuated manual insertion with a solid 11 gauge stylet into warmed (37 °C) pork hock bones. Force can be reduced by 50-60% by using the OsteoAccess System.

by attaching a load cell (Shimpo FGV-XY) to the hock bone. The OsteoAccess System's actuated insertion force was 62.5% of non-actuated insertion force (see **Figure 4**). Additionally, insertions were performed with a 13 gauge stylet and 11 gauge cannula. Five insertions were performed with non-actuated (manual) insertions and 4 insertions were performed with actuation (OsteoAccess). Insertion force was measured during each trial. Actuation statistically reduced the average force required to penetrate bone by 52 ± 8.3% (see **Figure 5**; Student's T-test, $p<0.001$).

PEDIATRIC INDICATION

Actuated Medical received a seed grant from the Philadelphia Pediatric Medical Device Consortium (PPDC) (*a center funded by the FDA*) - based at the Children's Hospital of Philadelphia (CHOP) - to evaluate the OsteoAccess System for pediatric bone biopsy and bone marrow aspirations [22]. In addition to the previously mentioned biopsy challenges, pediatric patients face the added risk of requiring general anesthesia, as this is a necessary measure due to the pain caused by the procedure [23, 24]. A lack of adequate samples, requires additional insertions and results in longer procedure times, extending the time the child remains under general anesthesia. Evidence in rodent and non-human primate models suggests that anesthesia has neurotoxic effects on brain development [25].

SUMMARY

Actuated Medical has developed a platform technology, the OsteoAccess System, to enable reduced force bone access of greater than 52 ± 8.3%. The reduced force enables oblique angled access. The oblique access enables improved clinician control, and provides more favorable paths for entry into the target tissue to diagnose cancer and other diseases. OsteoAccess' proprietary technology will enable low-force, angled penetration of rounded, hard surfaces where needles and drill bits tend to slip dangerously off the bone. The first commercial device will be the OsteoAccess-Biopsy for bone biopsy and bone marrow biopsy. The biopsy system will be followed by the development of devices for bone marrow harvesting, transplant, and intraosseous access. The OsteoAccess technology platform development has been funded by NIH/NCI SBIR grants.

These works are/were partially supported by the National Institutes of Health Small Business Innovation Research (SBIR) grant No. CA139774. The views, opinions and/or findings contained in this work are those of Actuated Medical, Inc. and should not be construed as an official government position, policy or decision unless so designated by other documentation.

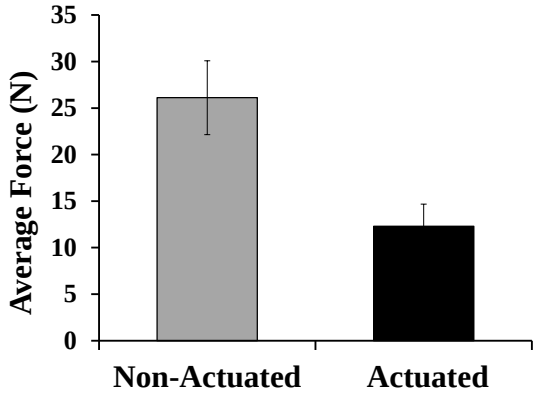

Figure 5: Insertion into warmed, hydrated porcine hock bones with 11 gauge cannula and 13 gauge stylet. Error bars indicate standard deviation, N=5 for Non-actuated, N=4 for Actuated. Insertions were performed within two minutes. Actuated insertions result in statistically significant reduction in insertion force (Student's T-test, $p<0.001$).

REFERENCES

1. HCUPnet: A tool for identifying, tracking, and analyzing national hospital statistics. http://hcupnet.ahrq.gov/HCUPnet.jsp. Accessed 3/1/11.
2. Liu PT, Valadez SD, Chivers FS, Roberts CC, Beauchamp CP. Anatomically based guidelines for core needle biopsy of bone tumors: implications for limb-sparing surgery. *Radiographics.* 2007;27(1):189-205; discussion 206.
3. Wu JS, Goldsmith JD, Horwich PJ, Shetty SK, Hochman MG. Bone and soft-tissue lesions: what factors affect diagnostic yield of image-guided core-needle biopsy? *Radiology.* 2008;248(3):962-970.
4. Clement RS, Bagwell R. Teleconference discussion of potential advantages of BIFOR technology on March 13 with Dr. Timothy Mosher.: Actuated Medical Inc; 2012.
5. Wilkins BS. Pitfalls in bone marrow pathology: avoiding errors in bone marrow trephine biopsy diagnosis. *J Clin Pathol.* 2011;64(5):380-386.
6. The Leukemia & Lymphoma Society - Fighting Blood Cancers. www.leukemia.org. Accessed October 26, 2010.
7. Frauenhoffer MD, Elizabeth. Personal Communication.
8. www.cancer.gov/images/cdr/live/CDR554337-750.jpg
9. Campbell J, Matthews J, Seymour J, Wolf M, Juneja S, Group ALL. Optimum trephine length in the assessment of bone marrow involvement in

patients with diffuse large cell lymphoma. *Ann Oncol.* 2003;14(2):273-276.
10. Bishop P, McNally K, Harris M. Audit of bone marrow trephines. *J Clin Pathol.* 1992;45(12):1105-1108.
11. Reid M, Roald B. Adequacy of bone marrow trephine biopsy specimens in children. *J Clin Pathol.* 1996;49(3):226-229.
12. Reid M, Roald B. Deterioration in performance in obtaining bone marrow trephine biopsy cores from children. European Neuroblastoma Study Group. *J Clin Pathol.* 1999;52(11):851-852.
13. Saghieh S, Masrouha KZ, Musallam KM, et al. The risk of local recurrence along the core-needle biopsy tract in patients with bone sarcomas. *Iowa Orthop J.* 2010;30:80-83.
14. Davies NM, Livesley PJ, Cannon SR. Recurrence of an osteosarcoma in a needle biopsy track. *J Bone Joint Surg Br.* 1993;75(6):977-978.
15. Bacci G, Briccoli A, Longhi A, et al. Treatment and outcome of recurrent osteosarcoma: experience at Rizzoli in 235 patients initially treated with neoadjuvant chemotherapy. *Acta Oncol.* 2005;44(7):748-755.
16. Bacci G, Ferrari S, Longhi A, et al. Therapy and survival after recurrence of Ewing's tumors: the Rizzoli experience in 195 patients treated with adjuvant and neoadjuvant chemotherapy from 1979 to 1997. *Ann Oncol.* 2003;14(11):1654-1659.
17. Kattapuram S, Rosenthal D. Percutaneous biopsy of skeletal lesions. *AJR Am J Roentgenol.* 1991;157(5):935-942.
18. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. Members of the Musculoskeletal Tumor Society. *J Bone Joint Surg Am.* 1996;78(5):656-663.
19. M. Mulvihill, D. Booth, B. Park, "Medical Tool for Reduced Penetration Force," U.S. Pat. No. 8,043,229 and U.S. Pat. No. 8,992,439.
20. P. Frankhouser, M. Mulvihill, B. Park, "Medical Tool for Reduced Penetration Force With Feedback Means", U.S. Pat. No. 8,328,738, U.S. Pat. No. 8,777,871, U.S. Pat. No. 8,777,944, U.S. Pat. No. 8,870,865, and U.S. Pat. No. 9,220,483; German Pat. App. No. 11-2009-002-245.4 (Filed 3/15/2011), China Pat. App. No. 200920144604.0 (Filed 5/10/2011).
21. P. Frankhouser, M. Mulvihill, R. Bagwell, R.S. Clement, G. Hernandez, R. Sheehan, B. Park, "Medical Tool with Electromechanical Control and Feedback," U.S. Pat. App. No. 13/371,310 (Filed 2/10/2012) and PCT App. No. PCT/US2012/024762 (Filed 2/10/2012).
22. Two companies to receive seed funds to develop medical devices for children. http://www.eurekalert.org/pub_releases/2016-01/chop-tct011316.php
23. Miller LJ, Philbeck TE, Montez DF, et al. Powered bone marrow biopsy procedures produce larger core specimens, with less pain, in less time than with standard manual devices. *Hematology Reports.* 2011;3(1).
24. Berenson JR, Yellin O, Blumenstein B, et al. Using a powered bone marrow biopsy system results in shorter procedures, causes less residual pain to adult patients, and yields larger specimens. *Diagnostic Pathology.* 2011;6:23.
25. Flick RP, H. IC. Anesthetic-Related Neurotoxicity in Children-ASA Works in Close Cooperation with FDA and Others to Advance Research. *American Society of Anesthesiologists.* 2015;79(3).