Contact:

Molly McDougall
HealthFlash Marketing
203-431-4000
molly@healthflashmarketing.com

Sharon Grutman
The American Society of Breast Surgeons
877-992-5470

Innovative Lymphedema Surveillance Program and Early Intervention Significantly Help Prevent Progression

Abstract: Interim Analysis Lymphedema "PREVENT" Trial

Dallas, May 2, 2019--Surveillance of women at risk for breast cancer-related lymphedema using bioimpedance spectroscopy (BIS) was more effective in preventing lymphedema progression than traditional arm circumference measurement, when each is combined with immediate compression therapy. These were the results of an interim analysis of 508 patients in a large, multi-site, international, randomized controlled trial comparing the detection of early lymphatic impairment using technology that directly measures extracellular fluid with conventional tape measure (TM) assessment. They were presented this week at the annual meeting of the American Society of Breast Surgeons.

"Breast cancer-related lymphedema is a chronic, debilitating swelling of the arm that may result from surgery, radiation, or chemotherapy affecting the lymph nodes. Lymphedema significantly lowers quality-of-life and consistently ranks as the number one fear of breast cancer survivors," says lead study author Sheila Ridner, PhD, RN, FAAN, Vanderbilt University School of Nursing.

She adds that this is the first trial of this type to demonstrate the efficacy of BIS over TM assessment to prevent progression of lymphedema through early lymphatic impairment detection, followed by immediate intervention with compression therapy using specially fitted sleeves and gauntlets.

"This study suggests that BIS is a highly effective tool for pinpointing patients at risk," Ridner says, noting that fewer women went on to develop clinical lymphedema when referred for therapy using BIS than TM.

The prospective study enrolled patients prior to cancer treatment who were undergoing mastectomy and/or a range of lymph node-related breast cancer surgeries, and/or radiation. After baseline measurements, patients were randomized to either the BIS or TM groups. Starting at 90 days post-

surgery, patients were regularly assessed and followed for a minimum of 12 months after surgery for this interim analysis.

TM patients who experienced an increase in arm circumference of 5% or more, reflective of subclinical lymphedema, were treated with compression therapy. For BIS patients, an increase of 6.5 L-DEX units from baseline, also reflective of a subclinical lymphedema, triggered therapeutic intervention. Therapy consisted of arm compression using a precisely fitted sleeve and chest gauntlet for 12 hours daily for 28 days.

In the study, 68 TM (28.5%) patients and 41 BIS (15.81%) patients or 21% of the overall participants met the thresholds and triggered interventions. The mean time to reach thresholds was 9.5 months for BIS and 2.8 months for TM. Ten TM triggering patients (14.7%) later progressed to clinical lymphedema requiring complex decongestive therapy versus two in the BIS group (4.9%). This represents a 67% relative reduction and a 9.8% absolute reduction (p=0.130) using BIS measurement. For both groups, clinical lymphedema was defined as a 10% increase in arm circumference with TM assessment.

Ridner notes that results were extremely encouraging. "These findings mean that women could potentially avoid this debilitating condition if BIS screening were the norm," she says.

Perhaps surprisingly, although more TM patients received early intervention, more also went on to suffer clinical lymphedema. Ridner explains that significant fluid accumulation is required for measurable increases in arm circumference. Additionally, TM assessment also includes fat, bone, soft tissue and other fluids that may result from the trauma of cancer treatment, complicating interpretation. Moreover, TM assessment leaves more room for human error. By contrast, BIS relies on electrical current to gauge fluid resistance between cells, providing extremely specific and precise measurement.

Ridner notes that BIS is a relatively low cost, fast, and non-invasive assessment tool. It not only potentially enhances patient care but also may save the significant expense of decongestive physical therapy if later required.

The clinical trial was launched in June 2014 and will follow all 1201 enrolled patients for three years post-surgery. Currently enrollment is complete, and 200 patients have completed the full protocol.

"I believe that this is a scientifically robust study," she says. "I expect that we will achieve similar results throughout the rest of the study and hope someday every breast cancer patient at risk will have access to this valuable tool."

Expert Commentary:

Lymphedema represents a significant morbidity for patients who experience it. This study demonstrates that bioimpedance spectroscopy can identify early signs of lymphedema so that interventions can be taken to prevent progression. This is an important step in improving the lives of our breast cancer survivors.

Julie A. Margenthaler, MD, FACS
Washington University School of Medicine, ASBrS Communications Committee Chair

Abstract, Official Proceedings

Interim Analysis Lymphedema "PREVENT" Trial

Authors: Sheila Ridner[1], Mary Dietrich[2], Andrew Moore[3], Michael Cowher[4], Bret Taback[5], Sarah McLaughlin[6], Nicolas Ajkay[7], John Boyages[8], Louise Koelmeyer[8], Sarah DeSnyder[9], Jamie Wagner[10], Vandana Abramson[11], Chirag Shah[12]

Institutions: [1]Vanderbilt University School of Nursing, Nashville, TN, [2]Vanderbilt University, Nashville, TN [3]Southeast Health Southeast Cancer Center, Cape Girardeau, MO [4]Alleghany General Hospital, Pittsburgh, PA [5]Columbia University, New York, NY [6]Mayo Clinic Jacksonville, Jacksonville, FL [7]University of Louisville, Louisville, KY [8]Macquarie University, Sydney, New South Wales, Australia, [9]The University of Texas MD Anderson Cancer Center, Houston, TX [10]University of Kansas Medical Center, Westwood, Kansas [11]Vanderbilt University Medical Center, Nashville, TN [12]Cleveland Clinic, Cleveland, OH

Objective: Breast cancer-related lymphedema (BCRL) represents a major source of morbidity amongst breast cancer survivors. Increasing data support the concept of early detection of subclinical BCRL followed by early intervention. A multi-site, international, randomized controlled trial is being conducted comparing lymphedema progression rates of those detected with using volume measurements derived from calculated from circumference using tape measure (TM) versus bioimpedance spectroscopy (BIS). We present results of a planned interim results.

Methods: Patients were enrolled pre-surgery and randomized to surveillance with either TM or BIS. Post-surgical inclusion criteria included Stage I-III invasive breast cancer or DCIS with at least 1 of the following: mastectomy, axillary treatment (axillary lymph node dissection (ALND), sentinel lymph node biopsy (SLNB) with greater than 6 nodes, axillary radiation), taxane-based chemotherapy. Additional post-surgical exclusion criteria included bilateral breast surgery. Patients who triggered intervention (change from pre-surgical baseline ≥ 5% volume by TM; ≥ 6.5 L-Dex BIS) were prescribed a compression sleeve and gauntlet for 4 weeks and re-evaluated. The trial's primary endpoint is the rate of lymphedema progression requiring complex decongestive physiotherapy (CDP) with progression defined as a TM volume change in the at-risk arm ≥ 10% above the pre-surgical baseline. This pre-specified interim analysis was performed when at least 500 trial participants had 12 months or greater follow-up.

Results: A total of 508 patients were included in this analysis who had been followed for least 12 months post-surgery (median=17.8 months, IQR=13-23). The median age was 58.8 years with 77% of patients (n=389) being white. Median Body Mass Index was 27.9 (IQR=24-33); the most frequently reported co-morbid conditions were cardiovascular in nature (44%, n= 223). A majority of patients were diagnosed with Stage I breast cancer (56.7%, n=288) with 39.0% (n=198) of patients having Stage II/III at baseline, the median baseline BIS measurement was 0.0 (IQR: -3 -+3.0) L-Dex units. Median arm volume in the at-risk arm at baseline was 1943.2 mL (IQR: 1685-2344) and 1949.6 mL (IQR: 1667-2335) in the non-at-risk-arm. Other than a single statistically significant difference in a history of digestive conditions, none of the key demographic, clinical, or baseline treatment characteristics differed

between the groups. Of the 508, 109 (21.9%) triggered pre-threshold interventions (n=68 TM group, n=41 BIS group). Compared to TM, BIS had a lower rate of trigger (15.8% BIS vs. 28.5% TM, $p<0.001$) and longer times to trigger (9.5 months BIS vs. 2.8 months TM, $p=0.002$). Twelve triggering patients progressed to CDP including 10 in the TM group (14.7%) and 2 in the BIS group (4.9%) representing a 67% relative reduction and a 9.8% absolute reduction ($p=0.130$).

Conclusions: Interim results demonstrate that post-treatment surveillance with BIS reduced absolute rates of progression of BCRL requiring CDP by approximately 10% compared with TM, although not statistically significant. These results may support the concept of post-treatment surveillance with BIS to detect subclinical BCRL and initiate early intervention.