somo•v® Automated Breast Ultrasound System

Physician Labeling

1. Manufacturer Contact Information

U-Systems, Inc.
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Sunnyvale, CA 94085
Toll Free: 866-364-6777

2. Prescription Use Statement

Federal law restricts this device to sale to or on the order of a physician. The use of this device is restricted to those who receive the appropriate training.

3. Indications for Use Statement

The somo•v® Automated Breast Ultrasound System (ABUS) is indicated as an adjunct to mammography for breast cancer screening in asymptomatic women for whom screening mammography findings are normal or benign (BI-RADS Assessment Category 1 or 2), with dense breast parenchyma (BI-RADS Composition/Density 3 or 4), and have not had previous clinical breast intervention. The device is intended to increase breast cancer detection in the described patient population.

4. Contraindications, Warnings and Precautions

A. Contraindications

There are no known contraindications for the use of the U-Systems Automated Breast Ultrasound System.

B. Warnings

There are no known warnings for the use of the U-Systems Automated Breast Ultrasound System.

C. Precautions

The safety and effectiveness of somo•v® Automated Breast Ultrasound System (ABUS) for breast cancer screening in women who have had a previous clinical breast intervention, such as surgery or biopsy, have not yet been scientifically studied. The performance of the device has been scientifically studied only when the ABUS images are read in conjunction with the patient's mammograms. If a lesion is visualized during the screening ABUS procedure, diagnostic ultrasound with a hand-held ultrasound device is recommended.

5. Clinical Study Summary

The U-Systems Pivotal Clinical Retrospective Reader Study (USI 2011001) [Pivotal CRRS] was a retrospective analysis of prospectively collected patient data obtained from an independent U-Systems Prospective Multi-Center Registry Study (USI 2008002) which is currently ongoing. The patient data was collected from a total of thirteen (13) investigational sites across the U.S. The retrospective analysis performed is an observational case-controlled, multi-reader, multi-case Receiver Operating Characteristic (ROC) study involving 17 Readers who were MQSA qualified radiologists with experience in breast image interpretation. There were 200 cases selected for the study from USI 2008002 of which 164 (31 were Cancer and 133 were Non-Cancer cases) were included in the primary analysis.

The primary endpoint analysis consisted of a Reader's image reading for a screening mammogram alone (XRM Alone) vs. the same Reader's image reading for the same screening mammogram paired with a screening ABUS exam from the same patient (XRM+ABUS). Using the area under the ROC (AUC), Readers performance with XRM alone compared to their performance with XRM + ABUS, was evaluated as a primary objective. The results of the Pivotal CRRS are summarized below and demonstrate the safety and effectiveness of the somo•v ABUS System to increase breast cancer detection.

A Reader first interpreted the screening mammograms of a case (XRM alone), and provided an XRM alone reading. Upon completing the XRM alone interpretation, the Reader reviewed the ABUS exam together with XRM, and provided a second reading for XRM+ABUS. The primary endpoint was the difference in the reader-averaged area under the ROC curve (AUC) between XRM alone reading and XRM+ABUS reading. A secondary endpoint was the Reader-averaged sensitivity and specificity for XRM+ABUS reading compared to XRM reading alone.

The following conclusions are based upon the results of the CRRS investigation. These conclusions were obtained from a population of 132 Non-Cancer cases with no prior breast interventions, 1 Non-Cancer case with a prior breast intervention, 15 Cancer cases with prior breast interventions and 16 Cancer cases with no prior breast interventions.

- ABUS read sequentially with XRM provides greater ability to detect cancer than XRM Alone for women with dense breast tissue who have a BI-RADS assessment of 1 or 2 with mammography, as evidenced by the significantly greater AUC.
    - Mean AUC across all Readers was 0.604 (95%CI: 0.536, 0.672) for XRM Alone and 0.747 (95%CI: 0.671, 0.822) for XRM+ABUS, yielding an estimated sequential read effect, $AUC_{XRM+ABUS}$ - $AUC_{XRM-ALONE}$, of 0.143 (95%CI: 0.074, 0.212; p<.001).

- ABUS read sequentially with the XRM provides an increase in sensitivity of 23.7% (95% CI: 10.0%, 37.9%; p=0.002): The overall sensitivity across all Readers was 38.5% for XRM Alone and 62.4% for XRM+ABUS, using a BI-RADS cut point 3.

    - ABUS read sequentially with the XRM provides an overall specificity across all Readers of 78.1% for XRM Alone and 76.2% for XRM+ABUS, yielding a change in specificity of -2.1% (95% CI: -8.0%, 3.8%; p=0.480).

- ABUS read sequentially with the XRM provides an increase in sensitivity of 31.0% (95% CI: 18.7%, 43.9%; p<.001): The overall sensitivity across all Readers was 27.1% for XRM Alone and 57.7%, for XRM+ABUS, using a BI-RADS cut point 4a.

  - ABUS read sequentially with the XRM provides an overall specificity across all Readers of 88.0% for XRM Alone and 84% for XRM+ABUS, yielding a change in specificity of -4.2% (95% CI: -9.3%, 0.4%; p=0.106).

- Sensitivity calculations at the tumor location level were repeated for each BI-RADS cut point. In addition to indicating a BI-RADS value above that of the cutoff threshold, the Reader must also have indicated the correct location of the tumor in order for the assessment to be counted as a hit. Since the indication of correct location only affects the proportion of true positives, specificities remain unchanged for the location-specific analyses.

  - Using a BI-RADS cut point 3, the location-specific sensitivity across all Readers was 23.0% for XRM Alone and 51.6% for XRM+ABUS, yielding an increase in sensitivity of 28.4% (95% CI: 16.5%, 41.8%; p<.001) when the ABUS is read sequentially with the XRM.

  - Using a BI-RADS cut point 4a, the location-specific sensitivity across all Readers was 18.8% for XRM Alone and 49.9% for XRM+ABUS, yielding an increase in sensitivity of 30.9% (95% CI: 19.4%, 43.8%; p<.001) when the ABUS is read sequentially with the XRM.

6. <u>Revised Clinical Study Summary: Excluding all cases with prior clinical breast interventions</u>

The selection criteria of the clinical study differed for cancer and non-cancer subjects. Specifically non-cancer subjects were excluded if the patient had prior breast interventional procedures. However, there was 1 non-cancer patient with prior breast intervention. In contrast, cancer subjects were excluded only if a prior breast intervention had occurred within one year prior to examination. It is noted that 15 of 31 (48%) cancer subjects had prior breast interventions more than 1 year prior to examination.

The results in Section 5 were obtained from a population of 132 Non-Cancer cases with no prior breast interventions, 1 Non-Cancer case with a prior breast intervention, 15 Cancer cases with prior breast interventions and 16 Cancer cases with no prior breast interventions. Note that according to the indications for use the intended use population corresponds to subjects without prior clinical breast interventions.

In order to address the limitation of having different selection criteria for cancer and non-cancer patients and to align the study population with the intended use population in the Indications for Use (IFU), a revised analysis was subsequently conducted on the Cancer cases and Non-Cancer cases that had no prior clinical breast interventions. The revised analysis and conclusions below align with the intended use population in the IFU. These revised conclusions were obtained from a population of 132 Non-Cancer cases with no prior breast interventions and 16 Cancer cases with no prior breast interventions.

- ABUS read sequentially with XRM provides greater ability to detect cancer than XRM Alone for women with dense breast tissue who have a BI-RADS assessment of 1 or 2 with mammography with no prior breast interventions, as evidenced by the significantly greater AUC.
    - Mean AUC across all Readers was 0.566 (95%CI: 0.472, 0.662) for XRM Alone and 0.782 (95%CI: 0.676, 0.888) for XRM+ABUS, yielding an estimated sequential read effect, $AUC_{XRM+ABUS}$ - $AUC_{XRM-ALONE}$, of 0.215 (95%CI: 0.101, 0.330; p<.001).

- ABUS read sequentially with the XRM provides an increase in sensitivity of 35.7% (95% CI*: 17.8%, 54.0%; p<0.001): The overall sensitivity across all Readers was 32.4% for XRM Alone and 68.1% for XRM+ABUS, using a BI-RADS cut point 3.

    - ABUS read sequentially with the XRM provides an overall specificity across all Readers of 78.1% for XRM Alone and 76.0% for XRM+ABUS, yielding a change in specificity of -2.0% (95% CI*: -7.9%, 3.9%; p=0.520).

- ABUS read sequentially with the XRM provides an increase in sensitivity of 42.1% (95% CI*: 24.8%, 59.7%; p<0.001): The overall sensitivity across all Readers was 22.1% for XRM Alone and 64.2%, for XRM+ABUS, using a BI-RADS cut point 4a.

    - ABUS read sequentially with the XRM provides an overall specificity across all Readers of 88.1% for XRM Alone and 83.9% for XRM+ABUS, yielding a change in specificity of -4.2% (95% CI*: -8.9%, 0.8%; p=0.094).

- Sensitivity calculations at the tumor location level were repeated for each BI-RADS cut point. In addition to indicating a BI-RADS value above that of the cutoff threshold, the Reader must also have indicated the correct location of the tumor in order for the assessment to be counted as a hit. Since the indication of correct location only affects the proportion of true positives, specificities remain unchanged for the location-specific analyses.

    - Using a BI-RADS cut point 3, the location-specific sensitivity across all Readers was 15.0% for XRM Alone and 56.5% for XRM+ABUS, yielding an increase in sensitivity of 41.5% (95% CI*: 21.5%, 61.9%; p<.001) when the ABUS is read sequentially with the XRM.

    - Using a BI-RADS cut point 4a, the location-specific sensitivity across all Readers was 13.1% for XRM Alone and 55.4% for XRM+ABUS, yielding an increase in sensitivity of 42.3% (95% CI*: 23.0%, 61.6%; p<.001) when the ABUS is read sequentially with the XRM.

* Point estimates and 95% Confidence intervals were derived from 1000 bootstrap samples respecting the proportions of Cancer and Non-Cancer cases, and considering Readers and cases as random.