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December 19, 2006


Michael Galperin, Ph.D.
Almen Laboratories, Inc.
1672 Gil Way
Vista, CA 92084

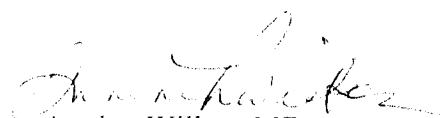
Re: Evaluation of Breast Companion software

Dear Dr. Galperin,

We were pleased to serve as principal investigators on the TJU evaluation of Almen Labs' software known as Breast Companion under the project entitled "Assessment of CAD System for Breast Cancer Diagnosis." This letter and associated documentation constitutes our final report for this important project. Our findings are attached to this letter and we look forward to future mutually beneficial collaborative efforts.

Yours sincerely,


Flemming Forsberg, PhD
Professor of Radiology
Head of Research, JUREI


Annina Wilkes, MD
Clinical Assistant Professor of Radiology
Head of Breast Imaging

1. Data for the evaluation

The department of Radiology, Thomas Jefferson University (TJU) retrieved 80 biopsy-proven breast cases from the PACS records of calendar year 2005 at the TJU Breast Imaging Center. The distribution of findings was:

- a. 6 fibrocystic changes (8 %)
- b. 21 fibroadenomas (26 %)
- c. 20 miscellaneous benign breast lesions (26 %)
- d. 27 invasive breast carcinoma (34 %)
- e. 6 miscellaneous breast malignancies (8 %)

Criteria for inclusion in the sample database were:

- a. Patient had a diagnostic ultrasound study as part of routine clinical care.
- b. A BIRADS score had been assigned to each patient's study.
- c. Patient had a breast biopsy and a complete pathology report.
- d. Ultrasound images were complete, of good quality, with minimal artifacts, no caliper graphics, no Doppler tracings, and all margins of the mass were completely contained in the image field.

2. Protocol for the evaluation

A single representative ultrasound image from each case was selected for review. A senior radiologist with subspecialty expertise in breast imaging reviewed the 80 breast ultrasound images with the Breast Companion™ (BC) following a training session with an experienced BC user. The images were first scored by the radiologist using a 5-point scale (definitely benign, probably benign, ... , definitely malignant). Then the radiologist segmented (i.e., outlined) the margins of the mass using the manual tool or if preferred, the automatic segmentation tool in the BC. The mass was characterized (i.e., scored) using the segmentation outline with the BC.

The final data sheet contained the original BIRADS score, the assessment of the radiologist and the BC score. The validity of the BC imaging diagnosis, the radiologists' assessment and the original BIRADS score was analyzed using logistic regression and receiver operating characteristics (ROC) analyses. Differences between ROC curves were tested by computing Mann-Whitney statistics.

3. Results

The area under the ROC curves (A_z) is listed in Table 1 together with its standard error (SE) and the associated p-value. The area under the ROC curve may be considered as the accuracy of the observation compared to the reference standard (here pathology). The first row in the Table represents the accuracy ($A_z = 0.70$) of the BIRADS categories found in the original radiology report for the 80 cases in the database. The radiologist in this study achieved an accuracy of 0.78, while the accuracy of the BIRADS score provided by BC from the segmentation outlines drawn by the radiologist was significantly higher ($A_z = 0.87$; $p < 0.0001$). The corresponding ROC curves are shown in Figure 1.

Table 1. Area under the ROC curves and the associated statistics.

Curve	Area	SE	p
Original Rad Score w/o BC	0.701	0.0622	0.0006
Rad BC Score no training	0.784	0.0525	<0.0001
BC auto with training	0.865	0.0452	<0.0001

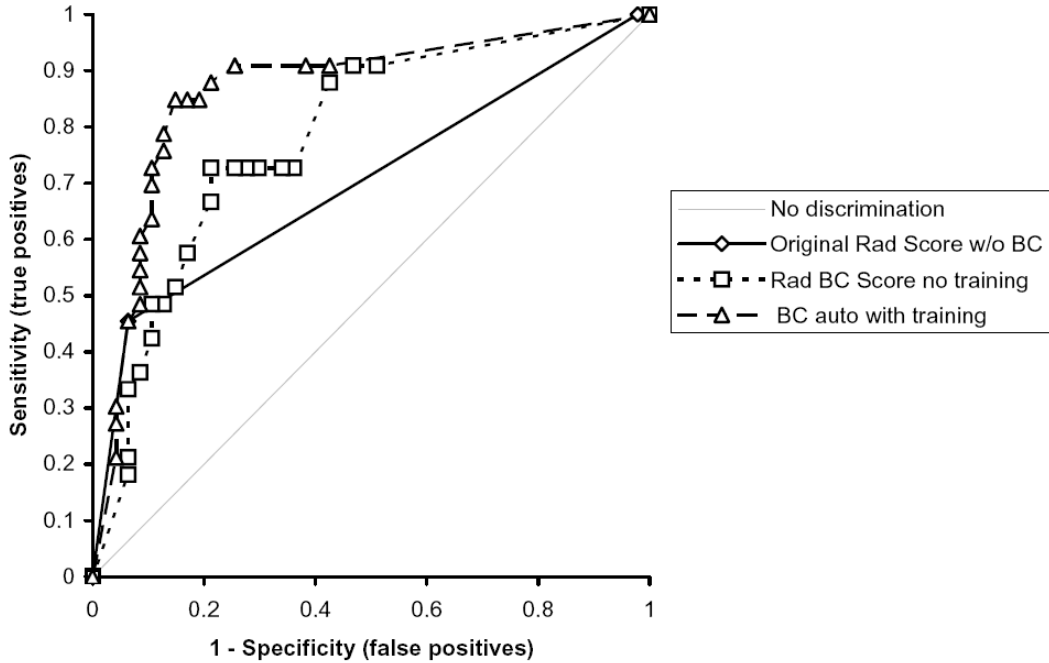


Figure 1. The ROC curves determined from the TJU data set.

4. Ease-of-use of the BC software

Since the BC software has several components, ease-of-use issues are addressed in each category.

- a. The procedural flow of the software is simple, appropriate and has an appealing "look and feel." The time to complete the analysis and report diminishes quickly with experience to less than 1 minute per case. The level of effort for an experienced user is acceptable although training in the use of the segmentation tools is clearly helpful.
- b. The report-generating feature of the BC software is well-designed and very easy to use. It follows the BIRADS reporting protocol accurately and uses the correct terminology. The style of completing the report is similar to that of other Radiology Information Systems so it is intuitive to use. Comments about the format of the report are offered in the next section.
- c. Although it is not difficult to perform the steps, users found segmentation to be the more challenging component of the BC analysis. Most masses were easily and accurately

segmented with either the automatic or manual tools. However, each user encountered several cases where segmentation was difficult to accomplish to the satisfaction of the user. This was mainly due to images where the mass produced heavy shadows or the mass was highly isoechoic with its surroundings. In some instances the manual segmentation produced unexpected results such that the user had to repeat the process a few times. Gaining experience with BC reduced the need to repeat segmentation.

5. Suggestions for future developments

- a. Provide means to manually edit segmented margins that are produced by automatic segmentation. Often the automatic segmentation is nearly perfect but normal shading and shadowing around a mass may require a minor edit to make it more accurate.
- b. Integrate BC in a radiology workstation to more seamlessly receive the DICOM image in question identified from a breast ultrasound image series in order to analyze it with BC. Ideally it would be desirable to mark the image in question, click a "BC icon" to transmit the image file to BC through some sort of imbedded application interface. Currently it serves well as an image analysis and reporting system but its intention is not to have complete tools for PACS review.
- c. The final report print layout is quite good, including the feature to allow the user to incorporate their logo. However, a means for the institution to design its own report format is required. Even more important for PACS and RIS users, it will be important in the future to provide a means to transmit the report in HLI7 text message format to the RIS or HIS to aid report generation.

6. Potential value of the BC software in clinical breast ultrasound practice

- a. The first expected benefit of using the BC software is the ability to implement a structured reporting system following the breast ultrasound BIRADS protocol. It is well known, that radiologists vary widely in their classification of breast masses using ultrasound. As a result, the American College of Radiology expanded the role of the Breast Imaging Reporting and Data System to include a structured lexicon and assessment system for breast ultrasound. At present this BIRADS ultrasound system is not as widely used as the mammography BIRADS.
- b. For radiologists who do not have an electronic reporting system the BC software can provide standardized reports. In addition the software has the potential to reduce inter- and intra-reader variability.
- c. The BC software may be especially attractive to radiology practices with lower volume of breast imaging procedures and practices where radiologists with breast imaging subspecialty are not available. In this setting BC provides an "expert second reader" to increase confidence in assessment of lesions.
- d. The BC may be modified to provide a quantitative assessment of breast tumor response to neoadjuvant chemotherapy. No such tool is currently on the market.
- e. The BC software may also become a valuable teaching tool for inexperienced users.