A Pilot Study in the Analysis of Digitized Mammograms
Combining Academic and Commercial Results on a Public Database

Melanie A. Sutton, PhD,* Sheri Sentelle, MS,† and Robert J. Rotunda, PhD‡

This article explores the development and utility of computer-assisted interpretation of mammograms with use of an academically developed mass enhancement system and the R2 ImageChecker M1000 System, a commercial mass detector system. This exploratory pilot study examines five mammogram views, three with abnormalities and two without, that were extracted from the public database known as the Digital Database for Screening Mammography. Digitized images were analyzed by an academic system (producing 25 different enhancement images) and original films were analyzed by the commercial R2 system (producing a set of five output views with region-of-interest prompts). Quantitative assessment was derived from radiologist-marked database ground truth information, whereas qualitative evaluation relied on a 210-question survey presented to two radiologists active in a breast cancer screening program. Academically developed segmentation-based enhancements appeared useful in aiding interpretation for the mass-prompting system by enhancing medically relevant features in prompt areas. Dual feature–based enhancements were preferred to single feature enhancements. Edge-based features appeared useful for facilitating clinical interpretation of possible spicules and for differentiating abnormal and normal tissues. This provisional study does not allow direct comparisons of the R2 system to other commercial or academic systems. However, this research does help to provide a framework for presenting medically relevant issues that can impact the development of digital mass-prompting systems and suggest alternative visualization techniques. [Key words: breast cancer, digital imaging, computer-aided interpretation, case study.] Journal of Women’s Imaging 2002;4:7–12

Learning Objectives: After reading this article and completing the posttest, the physician should be able to:

● explain the implications of using a public electronic database for basic research in digital mammography;

● explain the advantages and disadvantages of mass enhancement and mass prompting systems in digital mammography;

● list at least three different methods of image enhancement used to facilitate mammographic interpretation.

In 1999 alone, 43,300 women in the United States were expected to die from breast cancer.1 Although mammography is currently the single most effective method of early detection, the National Cancer Institute has increasingly supported interdisciplinary collaboration among scientists, mammographers, and industry to explore the development of better breast imaging technologies.2 Investigations into automation methods have also been driven by workload issues: typical screening rates suggest between 1.5 and 6 cancers will be uncovered for every 1,000 images viewed.3 Research groups in academia and the commercial sector have responded to this challenge by developing new electronic imaging systems and interpretation aids in the emerging field of digital mammography.

In the commercial sector, the ImageChecker M1000 System developed by R2 Technology (Sunnyvale, CA) is a calibration and mass-prompting system approved by the Food and Drug Administration.4 In this system, traditional mammogram films are scanned and then analyzed by marking two types of prompts or regions of interest (ROIs): clusters of bright spots (i.e., possible clusters of microcalcifications) and dense regions with radiating lines (i.e., possible masses or architectural distortions). Radiologists are expected to evaluate a traditional film mammogram displayed at eye level and then use prompts displayed on low-resolution monitors to verify or reevaluate their findings. Published evaluations of the R2 system have indicated that, on 285 cases from a screening population containing masses, 72.3% were correctly marked. On normal images, approximately 20% had no markers at all.5

There are also several alternative, nonprompting methods of facilitating interpretation at various stages in the clinical evaluation of a case. For example, segmentation as a diagnostic aid in the fight against cancer has a long history, including its use to enhance brain tumors.6 As a general process, image segmentation involves analyzing an image to reduce the number of distinct shades
of color or gray. For example, a segmentation algorithm applied to a mammogram image with 256 shades could reduce the number of shades to four, which might represent background or artifacts, muscle, fat, or tumors. This has the potential to help a clinician locate areas more easily and make more accurate assessments.

Along these lines, early software development work by Kallergi et al.\(^7\) used local thresholding and local region-growing segmentation methods to quantify and classify mammographic parenchymal patterns for the purpose of reducing variations in measurements. More recently, Pisano et al.\(^8\) analyzed an alternative use of segmentation in a study of the performance of various image processing techniques in digital mammography. The algorithm used an initial labeling of the mammogram into five different classes, providing labels for image areas representing background, uncompressed fat, compressed fat, dense tissue, and muscle. A mixture-model intensity windowing algorithm was then applied to the dense breast regions, to improve the visibility of lesion borders.

The funding constraints of early academic research and the proprietary nature of commercial system development has meant that systematic progress in the detection of breast cancer has often occurred on limited, non-shareable databases. As such, the algorithms’ repeatability, strengths, and weaknesses are difficult to assess. This pilot study addresses this issue by using a public database, the Digital Database for Screening Mammography (DDSM).\(^9\) This database contains 2,620 patient cases (each with four image views) with completely annotated ground truth information. An example case with ground truth outlines marking any abnormalities is shown in the top portion of Figure 1.

**Clinical Relevance**

With the use of a globally available database such as the DDSM, it becomes possible to build toolboxes of detection techniques with systematic testing against ground truth. With the additional participation of mammographers, it also becomes possible to elicit actual observer performance ratings to gather insights into the utility and acceptance of alternative visualization methods. This is similar to the approach used by Britton et al.\(^{10}\), which involved user preference studies of edge enhancements of hand images acquired by computed radiography. Within the mammography domain, this approach has also been described in work by Feig and Eskola-Feig\(^{11}\) who demonstrated clinical measures of sharpness, contrast, and conspicuity of early invasive cancers on hard copy, digital, and enlarged digital formats. Similarly, Pisano et al.\(^{12}\) asked radiologists to compare the visibility and “characterizability” of processed digital images of dense breasts to screen-film mammograms with use of a 5-point scale ranging from much better (+2) to much worse (−2).

Our approach differs from existing research in that we are eliciting such feedback based on cases from a shareable database with the goal of developing a multimodal approach to interpretation. Our methodology involves integrating prompt-based and enhancement-based information for a case, where such information is derived from commercial and academic systems, respectively. By specifically studying contrasting mass-enhancement and mass-prompting systems, we ultimately view the success of computer-aided diagnosis in mammography in the same manner as Pisano and Shtern,\(^{13}\) who have suggested that multiple display parameters for a given case are likely to be as useful as intensity windowing is for contrasting structural enhancements (i.e., soft tissue vs. bone) in computed tomography.

In addition, Mugglestone and Gale\(^{14}\) have speculated from work on visual search patterns that peripheral visual mechanisms will likely play an important role in mammography. These researchers examined visual search behaviors of clinicians who wore a head-mounted eye movement tracking system as they interpreted mammograms in their normal working environments and found that much of the visual information available on images is not assessed with high-resolution visual mechanisms. Kundel and Nodine\(^{15}\) also studied visual sampling strategies of radiologists and laypersons on a variety of images and speculated that ambiguous images contributed to a focus of visual attention on dominant pictorial features (e.g., borders, textured areas).

Segmentation of an image into various tissue classes is one method that provides data visualization that may be useful to peripheral visual mechanisms. The goal of segmentation as a tissue enhancement tool is to reduce the visual differences between similar image points so that acutely different areas (such as areas indicative of breast cancer) in different parts of the image more readily
prompt the clinician to examine those area(s) carefully. In this manner, the clinician might note structural similarities or differences in these areas that confirm and/or refute their understandings of possible confounds or features contributing to false negative, false positive, and true positive detections.

### MATERIALS AND METHODS

#### Case Profiles

The cases involved in this study were randomly selected from the subset of cases within the DDSM that were originally provided by the consultant radiologists working on this project. These cases were derived from three views with an abnormality and two views that were determined to be normal (i.e., that contain no abnormalities). The specific images used in this study are shown in Figure 2. A summary of the corresponding DDSM ground truth information, which includes a description of the standard Breast Imaging Reporting and Data System density and assessment ratings for these cases, is provided in Table 1.

#### Acquiring Digitized Mammograms for the Pilot Study

The R2 system contains a built-in film digitizer. To use this system, the original films associated with the DDSM case numbers in this study were placed in the single case loader processing unit. The films were then loaded into the motorized display unit of the system. The ROI prompts displayed on the low-resolution screens were then printed in the manufacturer’s format.

Alternately, the input to the academic mass enhancement system was a digitized image associated with each of the cases, downloaded from the DDSM public database site. The specific enhancement algorithm used in this pilot study was based on grouping the pixels composing each image into different tissue classes. Final pixel labels were based on analysis of either a single feature (intensity information) with use of five, seven, or nine different tissue classes.

### Table 1. Summary of Case Ground Truth Information (from DDSM)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>BI-RADS™ Density Description*</th>
<th>BI-RADS™ Assessment Rating†</th>
<th>DDSM Subtlety Description†</th>
<th>Lesion Shape Description</th>
<th>Lesion Margin Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2—scattered fibroglandular densities; some obscuring</td>
<td>4—suspicious abnormality</td>
<td>4—more obvious; interpretation easier</td>
<td>Irregular mass—cannot be characterized as round/oval/lobular</td>
<td>Spiculated—radiating lines</td>
</tr>
<tr>
<td>2</td>
<td>2—scattered fibroglandular densities; some obscuring</td>
<td>4—suspicious abnormality</td>
<td>4—more obvious; interpretation easier</td>
<td>Lobulated mass—contours with undulations</td>
<td>Ill-defined—poor margin definition; possible infiltration</td>
</tr>
<tr>
<td>3</td>
<td>1—breast is almost entirely fat; less obscuring</td>
<td>5—highly suggestive of malignancy</td>
<td>2—less obvious; interpretation harder</td>
<td>Oval mass—elliptical or egg-shaped</td>
<td>Ill-defined—poor margin definition; possible infiltration</td>
</tr>
<tr>
<td>4</td>
<td>3—heterogeneously dense; more obscuring</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>2—scattered fibroglandular densities; some obscuring</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* On a scale of 1–4.
† On a scale of 1–5.

**BI-RADS™** = Breast Imaging Reporting and Data System; **DDSM** = Digital Database for Screening Mammography; **Density** = a measure of the overall breast composition (tissue density) and implications for the sensitivity of mammography; **Assessment** = a measure of the overall impression of the lesion; **Subtlety** = a measure of the difficulty of the interpretation task.
classes (s5, s7, s9) or two features (intensity plus edge information), with seven or nine different tissue classes (d7, d9).

In all cases, segmentation was performed with use of the standard fuzzy c-means algorithm, an unsupervised least-squares clustering approach. The basic premise of this algorithm is that an initial set of class prototypes representative of the various tissue classes assumed to be present in the image is iteratively updated until a final set of prototypes meeting a minimum distance criterion is settled on. Final colored output images were then printed on 21.5-cm × 28-cm (8.5-in × 11-in) sheets of paper. An example set of segmentation images based on a single feature is shown in Figure 3.

Assessment Plan

A simplified overview of our processing is provided in the bottom two portions of Figure 1. Digitized images were analyzed by the academic system (producing 25 different enhancement images), and original films were analyzed by the commercial R2 system (producing a set of five output views with ROI prompts). Quantitative assessment was derived from radiologist-marked database ground truth information, whereas qualitative evaluation relied on a 210-question survey presented to two radiologists active in a breast cancer screening program.

There were 54 questions per abnormal case and 24 questions per normal case. All rating questions involved a 5-point scale, ranging from not useful at all (+1) to highly useful (+5) for aiding the interpretation task. Specific evaluation questions included rating each of the provided images on how well it enhanced or improved various dimensions such as architecture of the normal breast tissue; differentiation between normal and abnormal tissues; abnormal shape, size, or margins; tissues in the vicinity of and internal to the abnormality; speed of interpretation; and ability to highlight medically relevant and helpful information for interpretation. Commercial outputs were rated to determine the utility of ROI prompts for the given case. A final ranking question associated with each case involved selecting a preferred subset of useful images and ordering the subsets from most preferred to least preferred.

Image orders were randomized to avoid bias and intuitive trends in the image sequences. Space was also provided on the survey for the radiologists to explain or justify their ratings by defining medically relevant information for the given case or listing factors that facilitated the interpretation task. The survey questions were also grouped such that side-by-side ratings were elicited for different parameter sets of the mass-enhancement system. The results were analyzed for overall intrarater agreement, mean ratings for each algorithm evaluated, and radiologists’ preferences for a subset of images considered helpful as interpretation aids. The goal of this analysis was to determine the utility of different enhancement parameters and to ascertain what types of academic outputs could facilitate the interpretation of the ROI prompts derived from the commercial mass-prompting system.

RESULTS

We first considered the image enhancements and outputs for which both radiologists agreed about the overall performance and which had been given a mean score greater than 3 (on a scale of 1–5), indicating increasing usefulness as an interpretation aid. As summarized in Table 2, this agreement occurred in cases 1 and 2 for the academic system and in cases 2 and 4 for the commercial system. The overall intrarater agreement across all five cases, as reflected by Kendall’s τ-b, was 0.42 (P < 0.01). This suggests a fair to moderate level of overall agreement between raters and reflects alternative fact-finding strategies used by the radiologists during interpretation.

Table 2. Summary of Case Enhancements with Mean Ratings Greater than 3

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Image Output</th>
<th>Rating (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Radiologist A</td>
</tr>
<tr>
<td>1</td>
<td>d7</td>
<td>3.5 ± 1.0</td>
</tr>
<tr>
<td>1</td>
<td>d9</td>
<td>3.5 ± 1.0</td>
</tr>
<tr>
<td>2</td>
<td>d9</td>
<td>3.6 ± 1.7</td>
</tr>
<tr>
<td>2</td>
<td>r2</td>
<td>5.0 ± 0.0</td>
</tr>
<tr>
<td>4</td>
<td>r2</td>
<td>3.7 ± 1.2</td>
</tr>
</tbody>
</table>

d7/9 – dual feature enhancement with 7 or 9 tissue classes; r2 – commercial prompt-based output; n – number of survey items.
ditional details on interrater agreement for each algo-

rithm within the various cases is provided in Table 3.

For case 1, the more obvious spiculated mass embedded in fibroglandular tissue, this type of agreement occurred only on the dual feature enhancements (d7 and d9). For this case, the radiologists also agreed that these dual feature images would be useful within an interpretation aid subset because these enhancements helped visualize the spiculated mass and related architectural distortion. The commercial output for case 1 contained zero true positives and one false-positive prompt that was rated as not useful by both radiologists. Given that the commercial system is specifically designed to detect dense regions with extensive spiculated lines, the false negative in this case may be attributable to this constraint, because enhancements indicate a somewhat partial spiculation for the abnormality.

For case 2, the more obvious ill-defined mass embedded in fibroglandular tissue, both radiologists also agreed on the utility of the d9 enhancement. This enhancement was considered useful for enhancing the architecture of the normal breast tissues, the differentiation between normal and abnormal tissues, and the shape, size, and margins of the abnormality. This enhancement was also considered useful for providing helpful information for interpreting the patient’s mammogram. For this case, the commercial system output contained one true-positive and zero false-positive prompts and was also rated as helpful by both radiologists. For the interpretation aid subset, there was agreement that the commercial image followed by the d9 enhancement would be useful. Survey comments indicated that the ability of the academic enhancement to differentiate the abnormality from other tissues was valued.

The results are equally interesting for the normal image enhancements derived from case 4. Only the commercial image had a mean rating greater than 3 for this case. In addition, although the commercial output contained one false-positive prompt for this case, it was still ranked by both radiologists as useful within an interpretation aid subset.

Alternatively, for cases 3 and 5, the academic and commercial outputs received overall mean ratings lower than 3 (leaning toward the “not useful at all” end of the scale). Case 3, the more subtle ill-defined mass embedded in fatty tissue, was clearly the most difficult abnormal case to assess for both clinician and machine. The commercial output for this image contained zero true positives and one false-positive prompt, which was also rated as not useful and not providing helpful information for interpreting the patient’s mammogram. There was also no agreement on rankings of any useful interpretation aid subset, and comments by one radiologist indicated all outputs were useless. The normal image of case 5 also contained one false-positive prompt; however, both radiologists ranked the commercial output followed by the d9 enhancement as their two best images in an interpretation aid subset. Survey comments indicated this enhancement was ranked for its ability to enhance breast tissue architecture.

■ DISCUSSION

This pilot study explored the utility of alternative mass-
prompting and mass-enhancement systems that could help improve radiologists’ interpretations of digitized mammogram films and facilitate ROI prompt understanding. In addition, this study used a subset of images from the DDSM database, a globally accessible and shareable database, complete with ground truth information, and representative of the size needed if researchers hope to generalize their techniques to the large volume of data encountered in clinical screening programs.

Within the context of this specific pilot study, direct performance assessment of the commercial system compared to the academic system is clearly not possible and is not desired as a part of our evaluation methodology. The outputs provided by the academically developed algorithm and the commercial system are fundamentally different (enhancements vs. prompts) and involve different digitization methods. In addition, the R2 system has a built-in threshold of displaying no more than two mass ROI prompts per film. Alternatively, in the academic system, all image areas are equally targeted for enhancement. Additionally, the commercial system is specifically “tuned” to help clinicians detect spiculated masses, whereas the academic system is designed to enhance image areas representative of any type of abnormality.

Putting Together an Interpretation Strategy

In this pilot study, the radiologists consistently commented on the importance of enhancements that facilitated the discrimination of the abnormality, breast archi-

Table 3. Summary of Interrater Agreement by Algorithm and Case

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Exact Agreement on Algorithmic Outputs (%)</th>
<th>Moderate Agreement on Algorithmic Outputs (%)</th>
<th>Low Agreement on Algorithmic Outputs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>s5 s7 s9 d7 d9 r2</td>
<td>s5 s7 s9 d7 d9 r2</td>
<td>s5 s7 s9 d7 d9 r2</td>
</tr>
<tr>
<td>1</td>
<td>10 30 50 20 10 33</td>
<td>50 40 40 70 60 0</td>
<td>40 30 10 10 30 67</td>
</tr>
<tr>
<td>2</td>
<td>40 40 40 20 20 33</td>
<td>30 0 50 50 40 0</td>
<td>30 0 10 30 40 67</td>
</tr>
<tr>
<td>3</td>
<td>60 90 100 90 90 67</td>
<td>40 10 0 10 0 33</td>
<td>0 0 0 0 10 0</td>
</tr>
<tr>
<td>4</td>
<td>75 75 50 50 50 0</td>
<td>25 25 25 50 50 33</td>
<td>25 0 25 0 50 33</td>
</tr>
<tr>
<td>5</td>
<td>0 50 75 25 0 0</td>
<td>0 50 25 75 75 67</td>
<td>100 0 0 0 25 33</td>
</tr>
</tbody>
</table>

Exact Agreement = identical ratings; Moderate Agreement = ratings within 1 point on the 1–5 scale; Low Agreement = ratings at least 2 points apart on the 1–5 scale; s5/s7/s9 = single feature enhancement with 5, 7, or 9 tissue classes; d7/d9 = dual feature enhancement with 7 or 9 tissue classes; r2 = commercial prompt-based output. Number of ratings varied as a function of case and algorithm type. Percentages are based on 10 and 4 ratings for academic enhancements of abnormal and normal cases, respectively, and on 3 questions for commercial outputs.
tecture, or highlighted spicules. Overall, both increasing the number of features (from one to two) and increasing the number of tissue classes (from seven to nine) for the dual feature segmentation demonstrated the most potential in these areas. These results also appear to indicate that, although the radiologists may not always agree with the commercial R2 prompts, they seem to be comfortable with them and appreciate their utility as an interpretation aid in abnormal and normal cases.

One radiologist justified her rankings from an interface perspective, indicating a preference for the commercial outputs because the original image remained under the prompts, allowing the radiologist to register underlying breast locations more readily. This obviously saves time compared to scanning back and forth between different enhancement images, where different colors may be used in the same area across the subset. Additional survey comments also indicated color-based enhancements might be too distracting, given the traditional use of gray-scale in this field and in the commercial system. These factors likely contributed to the lower ratings for speed of interpretation with the enhancements compared to the commercial output. It may be possible to solve the registration problem with the incorporation of selected image tiles or landmarks in the segmented images that show underlying tissues from the original (unsegmented) images. Additional training of the radiologists on the benefits of color-based segmentations may also help to enhance comfort levels.

Inclusion of additional perceptual processing analysis will also be vital for developing algorithms that will augment a radiologist’s skill set, particularly for more difficult or ambiguous cases. In line with this, this descriptive series of case studies will next be expanded to include additional DDSM cases and clinicians to assess the utility of the dual feature segmentation enhancements on a broader set of data. We believe ongoing additional qualitative examination of procedures and assessment parameters will enhance progress in medical imaging, detection, and screening. In addition, although the images presented here were produced off-line, we are examining methods to generate them in real-time and extend algorithmic processing to microcalcification enhancement.

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References


Address correspondence to:

Melanie A. Sutton, PhD
Department of Computer Science
University of West Florida
1100 University Parkway
Pensacola, FL 32514
E-mail: msutton@uwf.edu