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Detection and Visualization of Inflammatory Breast Lesions Using Dynamic Contrast Enhanced MRI Volumes

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Abstract

Dynamic Contrast Enhanced MRI (DCE-MRI) is the acquisition of serial MRI images before, during, and after the administration of an MR contrast agent. [1] DCE-MRI has gained considerable attention for certain high risk cases such as dense breasts with smaller multi-focal lesions, sparsely distributed lesions, scarring after lumpectomy, evaluation following reconstructive surgery with implants, and/or discordant clinical and imaging data. DCE-MRI is used to characterize masses, stage tumors, monitor therapy non-invasively, and aid in the management of invasive disease [2]. DCE-MRI has a number of limitations, including overlap between malignant and benign inflammatory tissue, failure to resolve microscopic disease, and the inconsistent predictive value of enhancement patterns with regard to clinical outcome. In our study, we determined a confidence measure for each voxel in a DCE-MRI volume that represented the probability that the voxel was tumor or not, using a rough goodness-of-fit for the shape of the intensity-time curves. We used 3D texture mapping hardware to produce both 2D and 3D visualizations of the segmented MRI volumes in near real-time, enabling accurate spatial tumor information including location, shape, size, volume and distribution. To aid in staging and possible treatment courses, we produced statistical boundaries of the signal-time curves, for different tumor types and morphology and here we report the specifics of three cases of inflammatory breast disease using this system. We present preliminary results of our interactive computerized visualization system that aided in identifying, visualizing, and quantifying breast lesions from DCE-MRI volumes for inflammatory breast carcinoma. For one of these cases we imaged and analyzed the entire volume of breast pre- and post- chemotherapy. Using a “one-click” quantified approach to volume estimations of inflammatory malignancy, we demonstrated changes in apparent malignancy within breast parenchyma, both visually and quantitatively, using DCE-MRI, supporting the conclusion that DCE-MRI is useful in inflammatory breast cancer management.

Key words: MRI, DCE-MRI, inflammatory, breast cancer, confidence measure, texture mapping, volume rendering, invasive, discrimination, detection.

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Introduction

In conjunction with ultrasound, physical exam and needle biopsy, x-ray mammography is the current gold standard in clinical practice. However, its lower sensitivity in certain high-risk cases has been somewhat unsatisfactory [5,13]. In cases of dense breast parenchyma, following reconstructive surgery or assessing the volumetric extent of lesions, DCE-MRI sensitivity is superior [4]. Certain MRI protocols seem to yield higher probability of both higher sensitivity as well as higher specificity. The use of contrast agents, such as gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA), has demonstrated an increase in the sensitivity of MRI in certain protocols. DCE-MRI has been shown to help detect with increased sensitivity, certain types of cancer cells [2,3]

Two important factors have been suggested in enhancing tumor regions: (a) the effect of angiogenesis activity, resulting in increased vascularity or vessel density [4,7], and thus, increased contrast agent intake; and (b) increased vessel permeability, leading to increased leakage of contrast agent into the tumor site. Dynamic imaging of the breast makes it possible to analyze functionally the contrast *washin* and *washout* (WIWO), using signal-time curves [4] and there is reason to suggest that closer rigorous examination of the temporal dimension of these volumes might lead to higher specificity. Time-signal intensity curve [4] analysis has suggested that differing pathologies may yield differing curves [5]. However, direct visual examination of dynamic MR images with visual comparison is difficult at best, and is a time consuming and laborious task. With increasing spatial and temporal resolution in the acquired MR volumes, exhaustive manual processing and interpretation of dynamic MR volumes has quickly become infeasible. Additionally, there is considerable inter-observer and intra-observer variation in interpreting the enhancement of tumor regions [7]. A number of quantitative and estimation techniques have been proposed such as using the time delay between vessel and lesion enhancement [2], or using the percent enhancement beyond a certain time threshold. A second class of techniques focused on estimating the gadolinium concentration as a function of time, so as to extract pharmaco-kinetic parameters [5,15]. We asked whether analysis and interpretation of these signal-time curves would reveal useful information for location and type of lesion, particularly for inflammatory disease.

Method

We used a specific computerized algorithmic interactive visualization tool that we designed for the express purpose of evaluating DCE-MRI volumes. These kinetic curves were generated to examine the fit of empirical functions and parameters with reported pathological lesion classification. The algorithm computed signal-time curve data at each and every voxel in the entire breast volume, and from these data we computed a confidence measure, which represented the probability of malignancy, or not. The resulting confidence volume, in conjunction with the control volume (MRI volume without the contrast) was used to build a 3D texture. We used texture-mapped volume rendering techniques to view and interact with the MR volume in near real-time [5,6,11]. By adjusting the transfer function, we created semi-transparent renderings that displayed the suspected lesions (single or multi-focal) distributed

within the MR volume. Interactive viewing (rotation in all three dimensions, plus panning and zooming) allowed us to obtain a 3D perspective of each lesion, its location, shape, size, volume, orientation and distribution. Interactive manipulation and adjustment of various facets of the signal-time curves provided a means to deal with differing tumor characteristics. We present here three breast tumor cases involving inflammatory breast disease. We compared and correlated these findings to the surgical pathological findings from biopsy and resection.

Overall accuracy of these techniques has shown considerable variance in terms of lesion sensitivity and specificity, and thus has not gained wide acceptance to date. Even more complex, a single breast may contain more than one type of malignancy, adding complex variability to this inspection process. In our system, we have enabled interactive specification and modification of signal-time intensity curves followed by recalculation and display of cancerous sub-volumes over the entire breast volume. We suggest that near real-time volume visualization techniques for rapid analysis and quantification of breast lesions will increase hit values when normal tissues are mapped to shades of gray while cancerous regions are mapped to shades of red. In the 3D view, higher intensities and higher confidence values produce higher opacity (alpha) values.

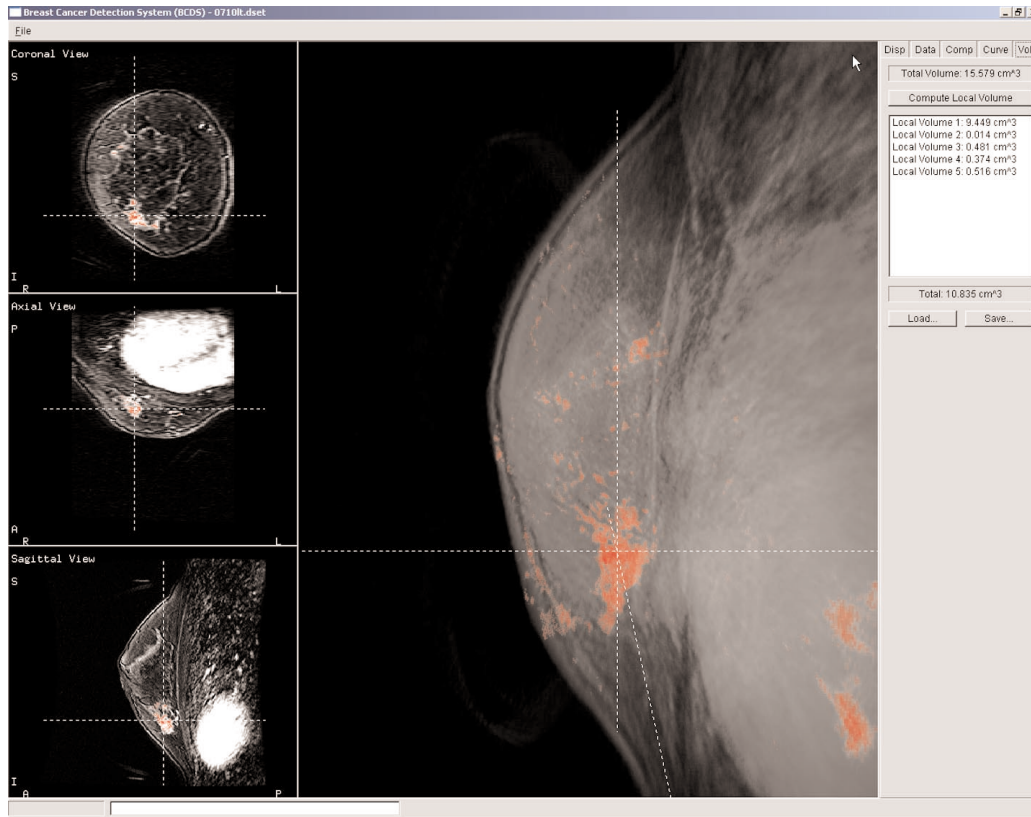
To compute the confidence measure for a particular voxel, we interactively specified a base signal-time curve that roughly reflected the shape corresponding to previously known cancerous lesions.

Series	Landmark	Image Mode	Plane	Pulse Sequence	VBW
3PL Loc	Xyphoid	2D	3-Plane	Localizer	Yes
Sag FSE	T2	Sternal	3D	Sagittal FSE-XL	Yes
T1 Special		Sternal	3D	Sagittal SPGR	Yes
3D Gado		Sternal	3D	Sagittal SPGR	Yes

Table 1: Breast MRI Protocol

Results

The results of this system can be seen in Figures 1-4, which represent various volumes of inflammatory breast cancer. In each Figure, three 2D linked panels are seen on the left, given 3D spatial localization within the volume while the interactive 3D view is shown in the middle of the Figures. On the right of the figures at the top is a white window that shows the calculated volume for each of the separate volumes within the breast, with the total measurement in cubic centimeters on the top and the calculated cubic measurement below the panel. Each was produced with a single “click” in the 3D panel for instantaneous measurement.



*Figure 1. Invasive ductal disease with inflammatory component
Case 1: 40 YO Caucasian female*

BCDDS report: At least five separate volumes with WIWO curve characteristics are highly suspicious for ductal invasive disease. These regions total 10.8 cu. cm. In the left lower outer breast there is a 3.0 cm seroma present in the prior biopsy site. And surrounding it is highly suspicious volume for residual malignancy extending over 3 cm in diameter.

Radiological Report: Left lower breast; there is a 3.0 cm seroma present in the prior biopsy site. Inferior to the seroma at the 6 o'clock position extending in the outer lower portion of the left breast 5 to 4 o'clock position near the chest wall, there is an abnormal regional enhancement present. This is highly suspicious for residual malignancy extending over 3 cm in diameter. Diffuse non-malignant like enhancement is present throughout the remainder of the left breast. No definite masses are detected in the upper breast. No lymphadenopathy is detected. No skin nipple or chest wall involvement is detected.

Pathology report: The residual DCIS and invasive carcinoma in the breast is felt to be residual as it is quite close to the previous biopsy pocket. Invasive tumor is present in block 13 that is an infiltrating ductal carcinoma high grade inflammatory. Summary 2 areas of invasive CA: Left axillary lymph node 1, metastatic carcinoma present; left axillary lymph node 2 metastatic carcinoma present summary: "infiltrating duct carcinoma, high grade, with extensive intraductal carcinoma (EIC tumor)"

Case 2: 57 YO Caucasian female
BCDDS report: Inflammatory breast cancer

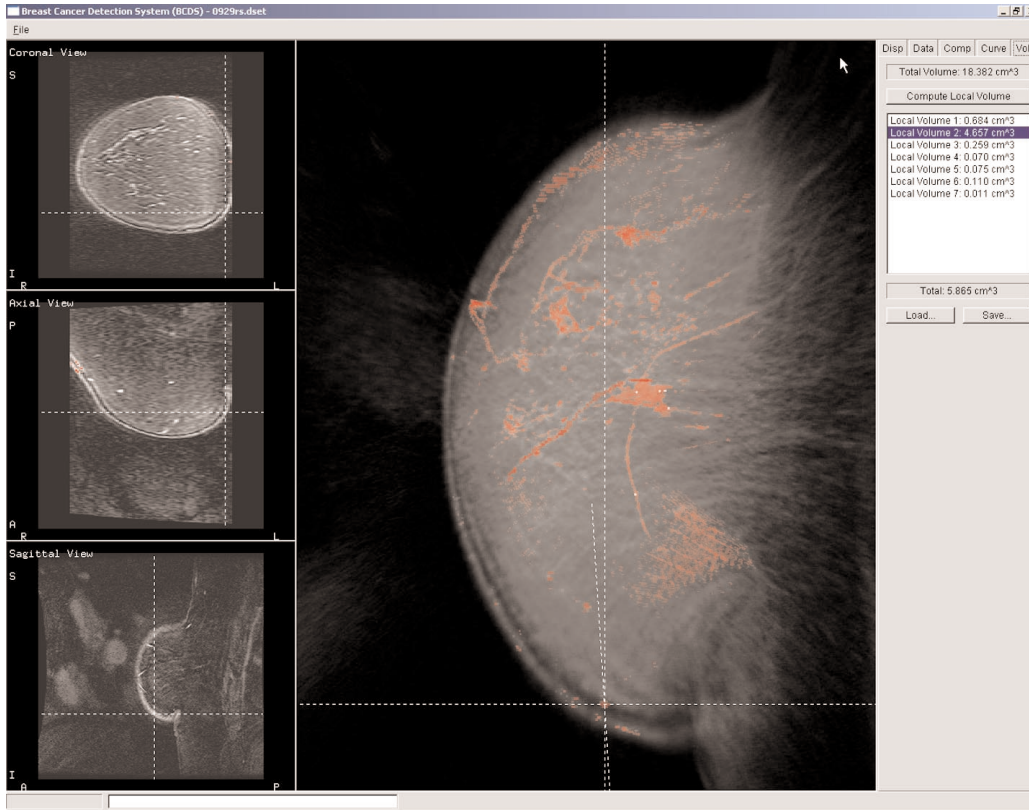


Figure 2. Diffuse inflammatory breast cancer

Case 3- Pre: 45 YO Caucasian female

BCDDS report: Inflammatory breast cancer: multi- focal disease with at least seven separate volumes totaling 5.865 cu. cm, ranging from 0.011 – 4.657 cu. cm, with WIWO curves indicating two types, two major locations, infiltrative, invasive ductal carcinoma

Radiological report: There is a relative paucity of fibroglandular tissue present. In the mid-aspect of the right breast just at the lateral side of the nipple there is architectural distortion and an approximately 1.5mm irregular soft tissue density. The soft tissue area is mildly hyperintense on T2 weighted sequences. In the more medial aspect of the right breast, superiorly, there is an approximately 4 mm moderately hyperintense focus.

After administration of Gad, there is fairly intense rapid enhancement with associated rapid

washout from the dominant right mid breast abnormality. This has irregular margins with associated architectural distortion and corresponds to the mildly hyperintense focus on the T2 weighted sequences. This probably represents a known focus of disease given the extent of abnormality and the architectural distortion in the region that may be related to the previous biopsy. The second smaller lesion in the upper inner right breast in zone 1 in approx R80 position does show fairly intense rapid washin and washout in a manner similar to the more dominant mass. This area is slightly larger on the post Gad images and mildly irregular in contour. It measures approximately 5 x 8 mm after Gad. Mildly hyperintense on T2 weighted images and not markedly hyperintense, it argues against a fibroadenoma and is concerning for a second focus of disease. The remainder of the right breast shows only minimal enhancement. No other suspicious areas are present. Two other nodules do not show progressive WIWO curves.

Pathology Report

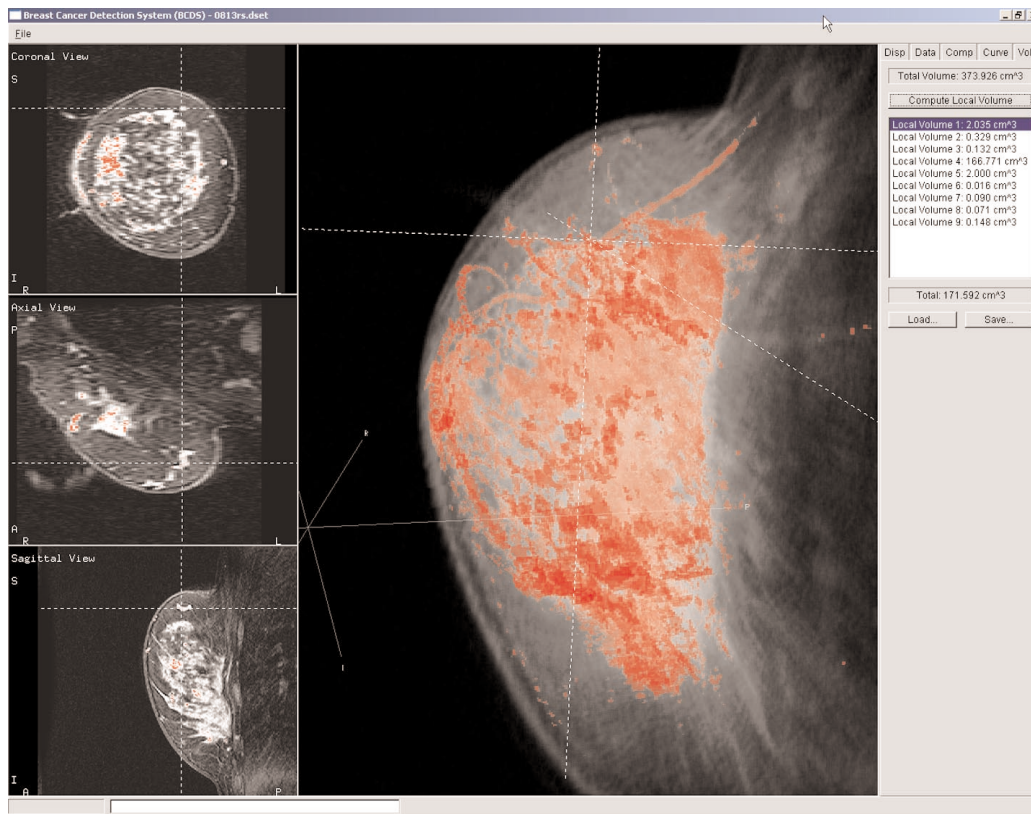


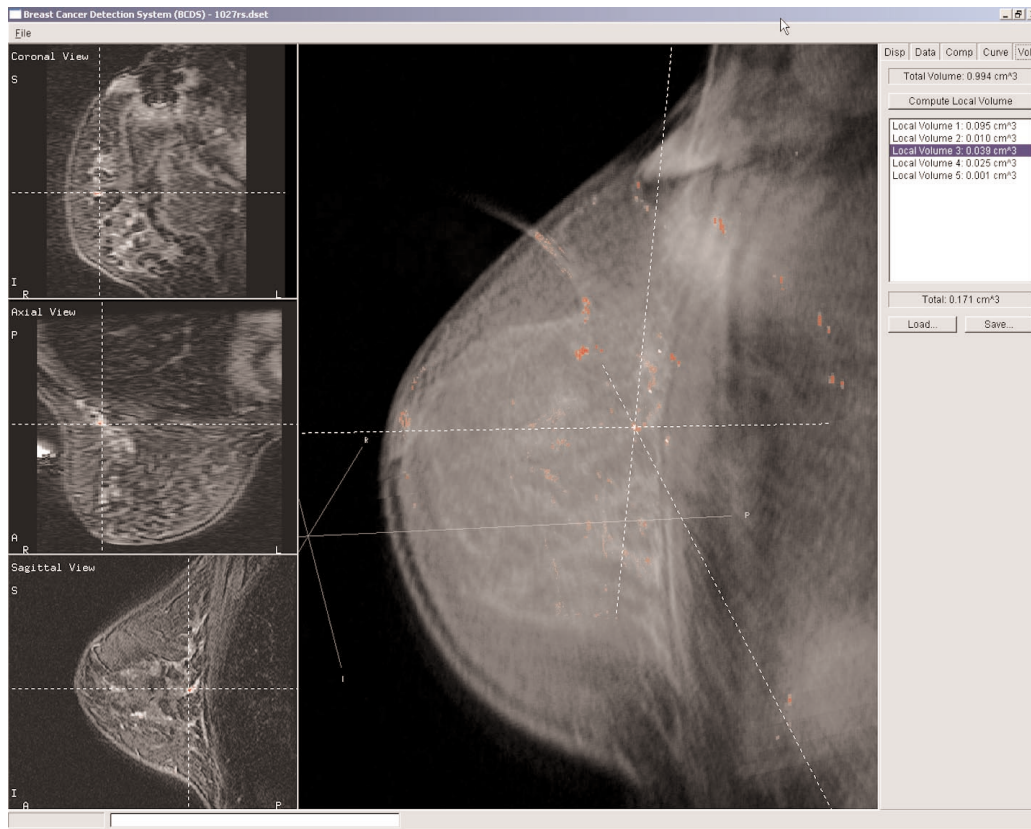
Figure 3. Extensive inflammatory Breast cancer prior to chemotherapy

Case 3- Post: 45 YO Caucasian female

BCDDS report: Inflammatory breast cancer

Radiological report: There is distension diffuse abnormal enhancement present throughout

the entire outer right breast but also involving portions of the right inner breast consistent with inflammatory breast cancer as stated in pts history. Difficult to measure lesion though it appears to measure greater than 7 cm in diameter. Enhancement extends to the nipple where there appears to be some skin thickening suspicious for nipple areolar involvement. There does not appear to be chest wall invasion



Pathology report: biopsy proven inflammatory breast carcinoma.

Figure 4. Inflammatory Breast cancer subsequent to chemotherapy

Case 3-Post: 45 YO Caucasian female

BCDDS report: Inflammatory breast cancer, in five volumes totaling 0.17. cu. cm. and ranging from 0.001 - 0.095 cu. cm.

Radiological Report: No inflammation, no rapid uptake nor washout. There is no change in the signal intensity curves that indicate any suspicious area or volume.

Small residual lymph tissue is suspected in several sites, particularly at R11.9 where there are 5

mm non-fat containing lesion is seen, but does not enhance post contrast.

Pathology report: no recent biopsy.

Discussion

This system provided an interactive visualization tool for assessing inflammatory breast lesions from DCE-MRI volumes. It provided an automatic exhaustive search of the 3D volume for suspicious tumor lesions by matching suspected WIWO characteristics. Discriminated volumes raise the potential for increasing hit rates while reducing errors of omission[7]. The visualizations consist of both 2D and 3D views: 3D views provide better characterization of shape and size, while the traditional 2D views provides more precise information about lesions in specific locations within the volume.. One disadvantage of these techniques is the high temporal resolution that is needed for maintaining accuracy, which in turn limits the size of the region being imaged. Our approach to using a confidence measure provides a probability measure that is easily adjustable and also provides an accurate means of computing tumor volumes. We tested our system on three cases of inflammatory breast carcinoma.

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