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Foreword: Imaging Techniques Alternative to Mammography for Early Detection of Breast Cancer

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Breast cancer is the most common cancer found in women today, with one in eight women in North America developing breast cancer during her lifetime. In the year 2004, it is estimated that there will be approximately 215,919 new cases of invasive breast cancer and about 40,110 deaths in the United States. Breast cancer is most effectively treated when detected at an early stage. Screening mammography is currently the primary imaging modality available for the early detection of breast cancer.

However, despite advances in mammographic techniques, it has a number of limitations. These shortcomings manifest themselves in the loss of 3D data associated with projection images (*i.e.*, overlying and underlying structures obscure features of interest in the projection radiographs), limits in sensitivity leading to an inappropriately high rate of “missed” cancers, and an intrinsic inability to prove that a suspicious abnormality is benign or malignant. Such deficiencies result in mammographers missing about 10% of all lesions. It is estimated that approximately two-thirds of these missed cancers are detected retrospectively by radiologists. In addition, about two-thirds of lesions sent to biopsy turn out to be benign, the overall yield of breast cancers per breast biopsy being roughly 10 to 50%. This has led to the investigation of alternative imaging modalities, such as magnetic resonance imaging (MRI), ultrasound, computed tomography (CT), *et cetera* for early detection and diagnosis of breast cancer.

While several medical imaging conferences incorporate various aspects of breast imaging, these have predominantly focused on mammography as well as associated image analysis techniques. Also, most medical imaging conferences offer a broad spectrum of medical imaging topics, with very few conferences focused primarily on breast imaging. Amongst the conferences focused on breast cancer, some are entirely focused on 2D mammography and others are more medically oriented, and hence do not cater to medical physicists, engineers, and scientists who work on developing alternate methods to image the breast.

The Workshop on Alternatives to Mammography was held in Winnipeg, Canada, September 18-20, 2004 to fill this void and to provide a forum to present and discuss these alternative breast-imaging modalities. Papers were presented by leading authorities in their respective areas and ranged from technical discussions on several currently used and experimental alternative imaging techniques to discussions on breast pathology, epidemiology, as well as associated image analysis techniques like computer-aided-diagnosis and image registration that may often be required to be used in conjunction with a certain imaging technique to produce more optimal results. Papers were presented in a collaborative atmosphere

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with plenty of opportunity for dialogue between researchers working on competing technologies. It is hoped that these dialogues will help push each technique to its limit and to foster a closer working-relationship and collaboration between these researchers. The modalities and techniques discussed in this workshop represent leading-edge methods for detecting and diagnosing breast cancer. It is hoped that ultimately such techniques will lead to improved early breast cancer detection, reduction of unnecessary biopsies, and improvements in early treatment protocols.

One of the aims of this workshop was to also distribute the information thus gathered to the wider community in the form of a special journal issue. This special issue of *Technology in Cancer Research and Treatment* serves this purpose. A number of papers presented at the Winnipeg workshop are included in this issue, with remaining papers to be included in a subsequent issue. All articles are peer-reviewed.

The first paper in this issue, which is by Pisano, reviews the use of screening mammography, including its current limitations and areas where it can be improved. The paper also outlines the steps needed and the process to be followed for any other modality to be accepted as a breast cancer-screening tool. The paper also enumerates several large-scale trials currently underway to evaluate mammography and competing imaging modalities.

Next, Vinh-Hung and Gordon establish a breast cancer tumor target size for new screening equipment and molecular detection. Using data from a public-use database, three different models were evaluated to study the effect of tumor size on breast cancer specific mortality. The best fit obtained with the lognormal model indicates tumor growth acceleration starting at about 2-3 mm. The authors thus conclude that the target size for breast cancer detection by current competing screening modalities should be 2 mm.

The third paper, by Tot, outlines the need for detailed and systematic mammographic-pathologic correlation for evaluating the benefits and pitfalls in mammography as well as to better evaluate the role of alternative breast imaging modalities. Large section histopathology is especially promoted as an ideal tool for this correlation. This review article describes different types of lesions as seen on mammograms and their ability to predict malignancy. Such information can be used to better correlate findings by an imaging modality and the final outcome as observed histologically.

Estimation of the size and shape of microcalcifications on mammograms (indicator of malignancy) is hindered because of overlapping information on a mammogram. The paper by Alto discusses the use of standard photogrammetry to better identify the 3D location of these suspicious regions in the breast. Using lead pellets (to simulate microcalcifications) embedded in an x-ray transparent Plexiglas phantom, the authors present results of the reconstruction of these using traditional photogrammetric techniques. These techniques are then applied to 2D mammographic films to generate a 3D depth map from which the location of suspicious regions can be better estimated.

The next paper, by Sivaramakrishna, provides a review of current techniques for breast image registration. Breast image registration applications include better visualization of lesions on pre- and post-contrast breast MRI images and lesions that can be characterized by growth relative to surrounding tissue as seen on longitudinal images. Image registration is also used in speckle tracking and image compounding in breast ultrasound images. It is also being increasingly used to align images arising from different imaging modalities, *e.g.*, alignment of positron emission and standard mammography images, ultrasound, and full-field digital mammography images, *et cetera*. It also has useful applications in monitoring cancer therapy. The focus of registration algorithms has shifted from control point-based semi-automated techniques, to more sophisticated voxel-based automated techniques that use mutual information as a similarity measure.

Next, Wood reviews the increasing use of computer-aided diagnosis in relation to breast MR imaging. Since 1999, there has been a 40 percent increase per year in the number of breast MR studies performed in the United States, with over 1200 sites having purchased breast surface coils for use in breast MR. Although MR has near 100% sensitivity for invasive breast cancers, radiologists have to use pharmacokinetic information coupled with morphological information to improve breast MR specificity. Automated CAD software plays a useful role here. CAD also helps radiologists process a large number of images in a relatively short time.

Weinberg *et al.* review Positron emission mammography (PEM) for early detection of breast cancer. PEM provides images of biochemical activity in the breast with high spatial resolution that allows visualization of intraductal as well as invasive breast cancers. This will allow PEM to complement anatomic imaging modalities in the areas of surgical planning, high risk monitoring, and minimally invasive therapy. In a related article, Reznik *et al.* describe an amorphous selenium-based PEM camera that provides a noninvasive highly sensitive and specific method for diagnosis of breast cancer with metabolic information that is not traditionally available in current anatomical imaging techniques. The PEM camera combines the high collection efficiency of lutetium oxyorthosilicate with the quantum efficiency, large avalanche gain, and rapid response time of amorphous selenium. The paper describes experiments to demonstrate the feasibility of the proposed camera.

Microwave imaging, in general, has gained a lot of interest in recent years because of significant advances in imaging algorithms, microwave hardware, and computational power. Microwave breast imaging has been of particular interest because the breast is relatively translucent to microwaves, is accessible for imaging, and its tumors appear to have a significant contrast with health tissues. In the next paper, Fear reviews the state-of-the-art in microwave imaging for breast cancer.

Suri *et al*. review a hybrid full field digital mammography and ultrasound (FFDMUS) system in development by Fischer in the next paper. The fusion of multiple modalities, in general, can effectively combine the best of each modality and offer increased specificity and sensitivity for lesion detection. The paper reviews the image quality of the ultrasound and X-ray system by evaluating the quality of lesion segmentation using novel techniques, in phantom images.

Finally, Diebold *et al*. present clinical results using Electrical Impedance Scanning (EIS) in 256 preoperative patients with BI-RADS™ III/IV/V-lesions. EIS uses the electrical conductivity and permitivity of lesions to differentiate between them. The authors discuss a level-of-suspicion (LOS) software that associates “spots” or detections using the EIS probe with a rating of malignancy using other patient-related information like age, *et cetera*. Although the overall sensitivity and specificity of this technique is still lower than mammography at this stage, the study demonstrates a higher sensitivity for smaller lesions with this technique. The paper states that better performance could be achieved by using higher frequencies for the scanner.