Editorial

Imaging in breast cancer – breast cancer imaging revisited

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In 2000, *Breast Cancer Research* published a series of articles describing the state-of-the-art of breast cancer imaging, edited by James Basilion [1-6]. This series reviewed developments in magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), radionuclide imaging with single-photon emission computed tomography (SPECT) and positron emission tomography (PET), and optical imaging, including optical computed tomography and near infra-red imaging fluorescence. The series had an emphasis on technical development, pre-clinical research, and early clinical studies. Five years later, we revisit the same areas of breast cancer imaging with an eye towards ongoing translational research and new opportunities to detect breast cancer early and to direct effective, individualized therapy.

Some of these imaging modalities have entered routine use in the clinic. Breast MRI is frequently used in the management of breast cancer, especially to determine the extent of disease in the breast and to direct local therapy [7]. ^{18}F-fluorodeoxyglucose (FDG) PET is increasingly used in staging advanced or recurrent breast cancer and in monitoring response to therapy and has received approval for Medicare re-imbursement for these clinical indications [8]. MRS and optical breast cancer imaging are not yet in routine clinical use, but increasingly compelling data in patients will likely to lead to more clinical use in the near future.

Lehman and Schnall [7] from the Universities of Washington and Pennsylvania provide a broad overview of the current and future uses of contrast-enhanced breast MRI. They review breast MRI imaging approaches that emphasized either temporal or spatial resolution. These approaches have been successfully merged to provide an optimal combination of sensitivity and specificity for breast cancer detection. New computer-based analysis methods may improve the ability to interpret the large volumes of data generated by dynamic contrast-enhanced MRI. The authors describe the use of breast MRI to direct local therapy and highlight work using MRI to measure primary or 'neo-adjuvant' systemic therapy. They review exciting recent work using breast MRI for screening high-risk women, showing the ability to detect lesions not found by mammography. As we continue to refine our estimate of a woman's individual risk of breast cancer, it is likely that breast MRI will play a role, perhaps complementary to mammography, in screening for high-risk patients. The development of newer and possibly more targeted MRI contrast agents may expand the capabilities of breast MRI.

Using much of the same technology needed for breast MRI, MRS provides a method for characterizing the chemical composition of breast cancer *in vivo*. Bolan, Nelson, Yee and Garwood [9] from the University of Minnesota review the technological issues and current state of breast MRS. Although MRS is frequently used in the clinical management of some tumors, such as brain tumors, breast MRS is just emerging as a clinically practical tool. Bolan and colleagues nicely describe the chemical and physical principles underlying breast MRS and the technical challenges of applying MRS to human breast cancer *in vivo*. The authors review technical developments, including higher magnetic fields, that have brought breast MRS to the point of being clinically practical. The authors review very interesting data on the ability of MRS to diagnose and characterize breast cancer in a way that is highly complementary to breast MRI. In addition, they highlight early but very promising work using MRS to monitor response to therapy, emphasizing that biochemical changes associated with disease response or progression precede anatomical changes (i.e., a change in tumor size).

Benard and Turcotte [8] from the University of Sherbrooke review the application of radionuclide imaging to breast cancer, including both SPECT and PET studies. Radionuclide imaging has long been used in breast cancer management, primarily in the form of bone scintigraphy ('bone scan') to detect bone metastases. The authors provide a thorough

CT = computed tomography; FDG = ^{18}F-fluorodeoxyglucose; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

review of SPECT and PET applied to breast cancer detection, regional lymph node metastasis detection, distant metastases staging, and therapeutic response assessment for both primary tumors and metastases. They review results in primary breast cancer detection with both SPECT and PET imaging agents, although this application has had only limited clinical use thus far. They highlight FDG PET for breast cancer staging and response to therapy, now routinely used in breast cancer care, emphasizing the complementary use of FDG PET and anatomical methods for these indications. As in MRS, the biochemical information provided by radiotracer imaging provides an early window to identify response to systemic therapy and may provide a quantitative endpoint for both clinical practice and clinical trials. The authors review preliminary studies using experimental radiotracers designed to image aspects of *in vivo* breast cancer biology beyond glucose metabolism and blood flow. This includes SPECT and PET methods to quantify estrogen receptor expression in breast cancer *in vivo* as a predictor of response to hormonal therapy. Hormonal therapy is perhaps the earliest form of 'targeted' cancer treatment, and estrogen receptor PET and SPECT therefore provide important paradigms for using imaging to direct breast cancer therapy by assessing the therapeutic target.

Tromberg, Carussi, Shah, Compton, and Fedyk [10] from the University of California, Irvine, review developments in optical imaging applied to breast cancer. They provide a thorough description of the methodology, emphasizing near-infrared imaging. They review specific approaches that have been applied to human breast cancer imaging, including diffuse optical imaging and diffuse optical spectroscopy. The authors nicely describe how optical imaging can be used to infer tissue properties of direct relevance to breast cancer care. They present early results using a prototype laser breast scanner to characterize breast lesions and describe a tissue optical index that indicates the likelihood that a particular lesion is malignant. Serial measures of optical indices can also be used to measure response to therapy. The development of robust, portable, and inexpensive devices holds great promise for making optical imaging a truly 'bedside' diagnostic tool that can contribute significantly to our ability to treat breast cancer.

It is important to emphasize that these newer imaging methods are complementary to existing imaging modalities, such as mammography and computed tomography (CT), and to each other. Lehman and Schnall emphasize that mammography and breast MRI have overlapping, but non-identical, sensitivity for clinically occult breast cancer, underscoring that the newer method, MRI, is a companion, not a replacement for, the existing and extensively tested older modality, mammography [7]. It is increasingly recognized that anatomical imaging and functional imaging work well together; this consideration led to the widespread use of imaging devices with both PET and CT capability (PET/CT) [8]. MRI and MRS can be used together without changing devices and are already used in combination for clinical management of some tumors. Bolan and colleagues [9] suggest compelling indications for the combined use of MRI and MRS in breast cancer. Preliminary studies show the complementary nature of PET and MRI in assessing response to primary systemic therapy [11]. MRS and PET are also likely to be quite complementary in measuring tumor biochemistry, since MRS measures biochemical pool sizes and PET measures the flux between different biochemical pools. Tromberg and colleagues [10] describe how optical imaging can be used routinely and repeatedly in the clinic or in the operating suite in a way that is highly complementary to the detailed and more geometrically extensive images generated by the other modalities. They provide specific examples of how optical imaging and MRI work well together.

A comparison of the 2000 and 2005 *Breast Cancer Research* imaging series suggests that we have made progress in moving newer breast cancer imaging modalities out of the laboratory and into the clinic; however, we have a lot more work to do. For applications like MRI and PET that have recently entered the clinical realm, we will need outcome and cost-effectiveness studies to decide how best to use these powerful, but often expensive, tools. For MRSand optical imaging, early clinical trials will help direct the use of these modalities in clinical research and clinical practice. In many cases, imaging will provide capabilities not previously available in the clinic, for example, the ability to assess the therapeutic target serially over the course of treatment, leading to new approaches for choosing and monitoring therapy. New treatments, for example, gene therapy, will need new imaging capabilities, such as imaging gene expression [2]. Advances in both human and animal imaging instruments will improve imaging's role as a facilitator of research translation. Imaging should serve increasingly as a tool for quantifying *in vivo* tumor biology in both animals and humans and for accelerating the transition from pre-clinical studies to early clinical trials to routine clinical practice. I look forward to the next *Breast Cancer Research* review series and the opportunity to report on more progress in using imaging to further our understanding of breast cancer and to improve the lives of breast cancer patients.

Competing interests

The author(s) declare that they have no competing interests.

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