

## RESEARCH HIGHLIGHTS

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#### Clinical Research

##### Procollagen Peptide May Predict Bone Metastases in Women With Primary Breast Cancer

Researchers from the United Kingdom and Finland presented the results from a study comparing bone marrow density and serum biochemical markers of bone turnover where bone-specific alkaline phosphatase, carboxy-terminal telopeptide of type I collagen, and n-terminal procollagen peptide of type I collagen (PINP) were analyzed at one and two years. A total of 498 women with breast cancer were entered in the trial and received either clodronate (a bisphosphonate that reduces osteoclast activity) (n = 243) or a placebo (n = 255). Bone marrow density was measured by dual x-ray absorptiometry at trial entry and annually. The researchers found a significant correlation between oral clodronate and an increase in mean bone marrow density in the spine and hip after two years. This increase was associated with a significant decrease in serum PINP. Patients in the control placebo group demonstrated a significant decrease in bone marrow density in the spine and hip. The serum PINP was significantly higher at one and two years in women who developed bone metastases during a median of 5.5 years of follow-up. The researchers concluded that serum PINP levels may be useful as an early marker of bone metastases and may help in selecting appropriate long-term treatment for patients with breast cancer.

##### Blood Test May Be Useful for Detecting Breast Cancer

Protein chip mass spectrometry is a technique used to identify multiple changes in protein levels to develop a profile of disease biomarkers. Researchers from Eastern Virginia Medical School in Norfolk used this technology to examine serum samples from 92 female patients. They used surface-enhanced laser desorption/ionization (SELDI) mass spectrometry to create protein profiles and a decision-tree algorithm and biomarker pattern software for classification analysis that yielded seven characteristic protein peaks. Fifty women were

diagnosed with breast cancer and 42 had benign lesions. The protein profile analysis demonstrated 85% specificity and 78% sensitivity. The researchers concluded that SELDI protein chip mass spectrometry of serum samples with appropriate classification can identify breast cancer with a specificity and sensitivity that approaches mammography. They recommended that a larger study is needed to confirm these results.

##### Visual and Digital Assessment of Changes in Breast Density May Be Clinically Meaningful

High breast density is associated with an increased risk for developing breast cancer. Although standards currently exist for assessing breast density, no standards define a clinically meaningful change in breast density. Researchers from the University of Virginia in Charlottesville presented results from a study using a visual and digital assessment of breast density. The study involved 28 postmenopausal women who had an increase in breast density related to hormone replacement therapy and 10 postmenopausal women who had no reported change in breast density. Mammograms were examined by an experienced radiologist and digitized using a high-resolution Lumisys 75 scanner. The radiologist classified cases from 0 to +3, depending on the degree of change in breast density. The visual assessment placed 9 cases in the +1 range (density increase of less than one breast imaging reporting and data system [BIRADS] category), 10 in the +2 range (increase of one BIRADS category) and 9 in the +3 range (increase of one or more BIRADS categories with an increase in breast size). Digital assessment recorded an average increase in density of 6.8% in the +1 group, 18.7% in the +2 group, and 37.4% in the +3 group. The digital assessment recorded a mean decrease of 1.4% in density in the control group. The researchers concluded that they have been able to define changes in breast density in clinically meaningful categories and that these correlate with quantitative digitally assessed changes.

#### Epidemiologic Research

##### Mammography May Detect Nonpalpable Breast Carcinomas With a High Cure Rate

The ability of mammography to increase long-term survival for patients with breast

cancer remains controversial. Researchers at the University of Southern California in Los Angeles compared survival data for 3,617 patients with breast cancer. Of these, 1,564 had nonpalpable lesions discovered by mammography (576 invasive and 988 in situ) and 2,053 had palpable lesions. The 10-year actuarial distant disease-free survival was significantly greater for all nonpalpable lesions compared to the palpable lesions (95%, 89%, and 73%, respectively). The overall survival also was better for the nonpalpable lesions compared to the palpable (89% and 84% for nonpalpable and 70% for palpable). The researchers concluded that mammography identification of suspicious areas leads to a biopsy-detected subgroup of patients with breast cancer who have a statistically superior cure rate compared to patients with palpable lesions.

#### Basic Research

##### Functional Genomics Breast Cancer Database Links Data Potentially Critical for Diagnosis and Treatment

Breast cancer is known to be a highly heterogeneous disease. Altered responses to inhibitory and proliferation signals, differentiation, apoptosis, and angiogenesis, as well as alterations in many other processes regulated by multiple genes, occur. Microarray technologies, where thousands of genes can be examined from a single tissue or serum sample, offer the possibility of establishing profiles of tumors fundamental to understanding the altered responses in carcinogenesis. Researchers from the National Institutes of Health in Bethesda, MD, described a comprehensive database generated from 14,000 genes that will offer information on in vivo tumor profiling, proliferation, drug sensitivity and resistance, hormonal impact, apoptosis, and epigenetic and post-translational regulation of differentiation. The database will serve as a link among clinical data, functional assays of cell lines, and online databases. It will prioritize and accelerate the search for genes that may have diagnostic, prognostic, or therapeutic values.

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