June 15th, 2022

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

This month I will cover "Using AI to Detect Breast Cancer". To read this article, go to the Table of Content and click on the link.

If you missed last month newsletter on "What's New in Robotics?", click on this link to read the article.

If you need a little inspiration or something to make us laugh to get us through this difficult time, click on the "Inspiration" link to give yourself a few minutes to relax and enjoy the music from the Berklee School of Music in their song "What the World Needs Now," other inspirations and ending with Celine Dion and Josh Groban with "The Prayer".

newsletter will be published on July 15th, 2022.

We encourage you to share this newsletter with your colleagues by using the social media icons below, or by simply forwarding this newsletter or use the link below. Should you or your colleagues want to join my mailing list, click on "join my email list" link below.

Please email me, Regina Au, if you have any questions, comments, or suggestions.

Sincerely,
Regina Au
CEO, New Product Planning/Strategic Planning
BioMarketing Insight

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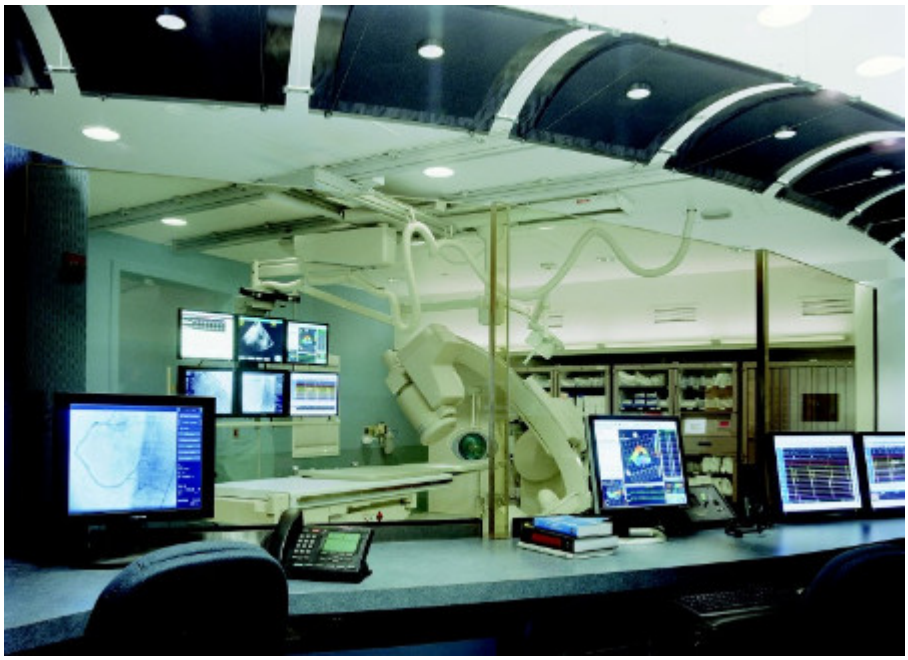
Join my mailing list



Developing a Product? Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact me for an appointment. For successful commercial adoption of your product or looking to grow your business, contact me for an appointment.

For more information on our services, click on the links below:

Product Development
Market Development
Marketing Strategies
Scenario Planning - for more information, email me.

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See Photos of the AAPI Heritage Festival - Saturday, May 7th, 2022

Asian American Pacific Islander (AAPI) Heritage month is a celebration of a diverse group of ethnic heritage within the Asian community who bring a wealth of enriched culture to our society. This celebration will endeavor to build awareness and educate our community on the various cultures and contributions these different Asian ethnic groups have brought to enrich our American Story.

History you may not know:

1. 20,000 Chinese men served in the military during WWII where 40% of the men served without American citizenship due to the "Chinese Exclusion Act".They were later honored in September 2021 with the Congressional Gold Medal for their acts of patriotism, loyalty, and courage for the US.
2. 110,000 Japanese American and Japanese were relocated to prison camps during the bombing of Pearl Harbor in 1941.In 1943, Japanese Americans were finally allowed to volunteer for the all-Japanese American 442nd Regiment that fought against the Japanese.These men were awarded the Congressional Gold Medal in 2010.

Theme: Contributions Asian American Pacific Islands Have Made to American History
A walk-through exhibit highlighting the contributions AAPI have made to American History was on display.

The Festival was a huge success with a full agenda of speakers, including State Senator Cindy Friedman and fireside chats with Shirley Leung from The Boston Globe. We also had a full agenda of performers throughout the festival. We had Tibetan dancers,

In addition, we had exhibitors from the various ethnic groups displaying items representing their history and culture that complemented the contributions that AAPI have made to American History.

This is AAPI Heritage month, be sure to enjoy all the activities in your area celebrating the diverse group of ethnic heritage within the AAPI community who bring a wealth of enriched culture to our society and American History. It may surprise you the tremendous amount of people who have contributed to our society and American History.

I would like to leave you with this **one thought** "while everyone is unique in their own way, it is important to celebrate our differences and our commonalities. Every person has a vital contribution to make to society - all races, all ethnicities, all religions and all genders together form one human race.

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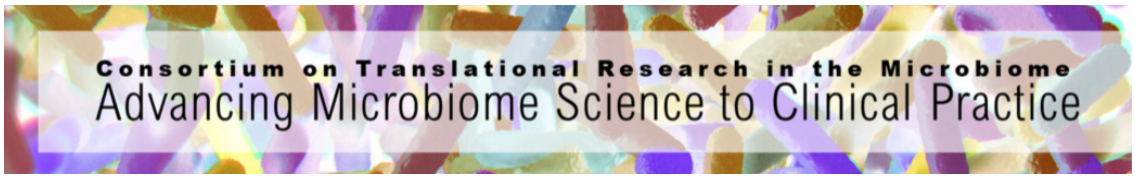

General Guidelines to Launch and Build a Clinical Trial Using Microbiome Products in an Era of Personalized Medicine.

I am pleased to announce that I was a speaker at the Westchester Biotech Project for Consortium on Translational Research in the Microbiome on November 11th, 2021. The Topic: General Guidelines to launch and build a clinical trial using microbiome products in an era of personalized medicine. My presentation was on " How to Launch and Market a Successful Microbiome Product: Five Major Considerations". For more information on this event, click here. This webinar it will be available next month, so check back here.

For more information on Westchester Biotech Project and future webinars, click here.

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imcusa
Institute of Management Consultants

Fresh Thinking in the Next Normal

I am pleased to announce that I was a speaker at the Institute of Management Consultants event on "What Will the “Next Normal“ Be for Productivity, Motivation and Retention of Employees? Four Things Employers Need to Consider." on July 20th, 2021 at 2 pm. For more information and to register click here.

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Enjoy the song "What the World Needs Now" virtually with the students from the Berklee School of Music.

We Will Get Through It Together

Let's End with Celine Dion & Josh Groban Singing "The Prayer"

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One Biotech Executive's View on the COVID-19 Vaccine

I am pleased to announce that my article on the COVID-19 Vaccine was published in Lioness Magazine. To read my article click on the link here.

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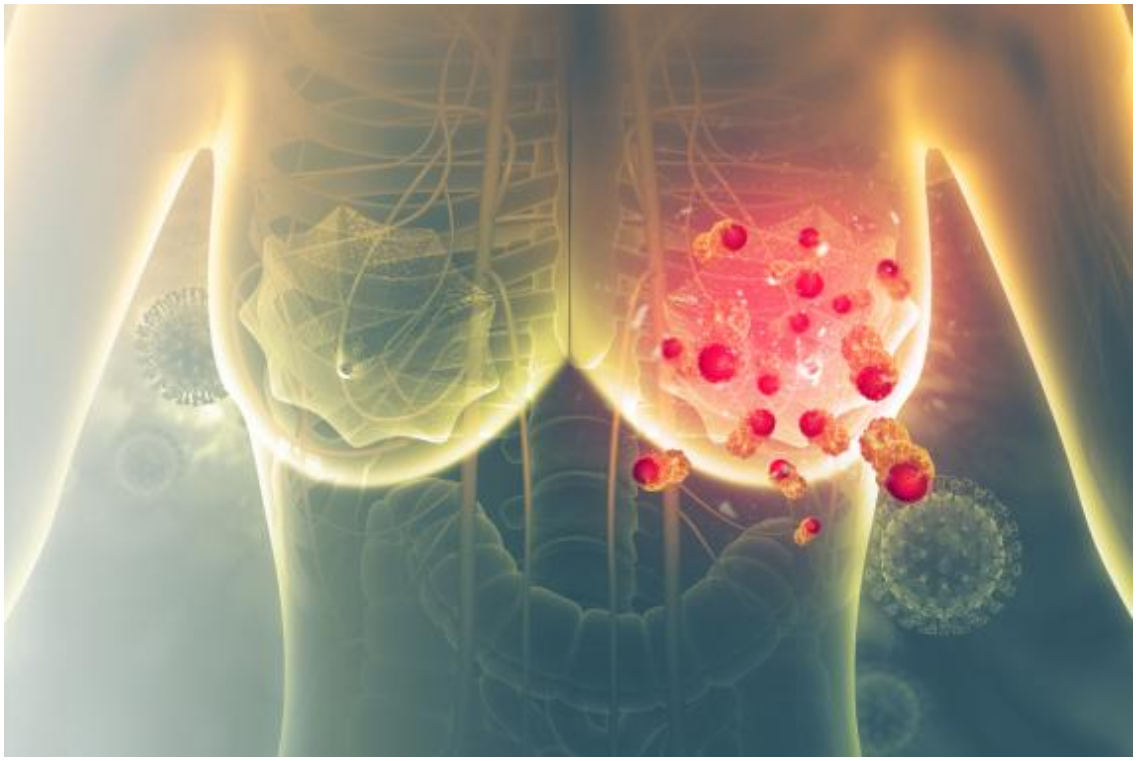


Using AI to Detect Breast Cancer

Source: Radiology Business: myuan, Tue, 03/03/2020

Breast Cancer Statistics

In the United States, about 255,000 cases of breast cancer are diagnosed in women and about 2,300 in men each year. About 42,000 women and 500 men in the U.S. die each

Black women with breast cancer have triple-negative breast cancer - more than any other racial/ethnic group and the most difficult breast cancer to treat successfully.

About 1 in 8 U.S. women (about 13%) will develop invasive breast cancer over the course of her lifetime. About 2,710 new cases of invasive breast cancer are expected to be diagnosed in men in 2022. A man's lifetime risk of breast cancer is about 1 in 833.

Cancer is the second leading cause of death, after heart disease, in the United States in 2020 and breast cancer in women is the fourth leading cause of death. Worldwide, **female breast cancer is the fifth leading cause of death**. In 2020, an estimated 684,996 women across the world died from breast cancer.

What are the causes of Breast Cancer?

Doctors estimate that about 5 to 10 percent of breast cancers in females are linked to gene mutations passed through generations of a family.

There are various types of breast cancer:

1. Angiosarcoma
2. Ductal carcinoma in situ (DCIS)
3. Inflammatory breast cancer
4. Invasive lobular carcinoma
5. Lobular carcinoma in situ (LCIS)
6. Paget's disease of the breast
7. Recurrent breast cancer

There are also risk factors that can contribute to breast cancer:

- **Being female.** Women are much more likely than men are to develop breast cancer.
- **Increasing age.** Your risk of breast cancer increases as you age.
- **A personal history of breast conditions.** If you've had a breast biopsy that found lobular carcinoma in situ (LCIS) or atypical hyperplasia of the breast, you have an increased risk of breast cancer.
- **A personal history of breast cancer.** If you've had breast cancer in one breast, you have an increased risk of developing cancer in the other breast.
- **A family history of breast cancer.** If your mother, sister or daughter was diagnosed with breast cancer, particularly at a young age, your risk of breast cancer is increased. Still, the majority of people diagnosed with breast cancer have no family history of the disease.
- **Inherited genes that increase cancer risk.** Certain gene mutations that increase the risk of breast cancer can be passed from parents to children. The most well-

cancer inevitable.

- **Radiation exposure.** If you received radiation treatments to your chest as a child or young adult, your risk of breast cancer is increased.
- **Obesity.** Being obese increases your risk of breast cancer.
- **Beginning your period at a younger age.** Beginning your period before age 12 increases your risk of breast cancer.
- **Beginning menopause at an older age.** If you began menopause at an older age, you're more likely to develop breast cancer.
- **Having your first child at an older age.** Women who give birth to their first child after age 30 may have an increased risk of breast cancer.
- **Having never been pregnant.** Women who have never been pregnant have a greater risk of breast cancer than do women who have had one or more pregnancies.
- **Postmenopausal hormone therapy.** Women who take hormone therapy medications that combine estrogen and progesterone to treat the signs and symptoms of menopause have an increased risk of breast cancer. The risk of breast cancer decreases when women stop taking these medications.
- **Drinking alcohol.** Drinking alcohol increases the risk of breast cancer.
- **Dense breast tissue** - Breast density is the amount of breast tissue compared to fat tissue in your breasts. If you have a high amount of breast tissue compared to fat, you have a 'high breast density'. This increases the risk of breast cancer. The denser the breast, the greater the risk. Breast density varies naturally between women and can only be measured on a mammogram.

In men, breast cancer is rare and it is not real clear on the cause except that it may be genetically related as well. There are three types of breast can in men.

- **Cancer that begins in the milk ducts (ductal carcinoma).** Nearly all male breast cancer is ductal carcinoma.
- **Cancer that begins in the milk-producing glands (lobular carcinoma).** This type is rare in men because they have few lobules in their breast tissue.
- **Other types of cancer.** Other, rarer types of breast cancer that can occur in men include Paget's disease of the nipple and inflammatory breast cancer.

There are also risk factors that can contribute to breast cancer in men:

- **Older age.** The risk of breast cancer increases as you age. Male breast cancer is most often diagnosed in men in their 60s.
- **Exposure to estrogen.** If you take estrogen-related drugs, such as those used for hormone therapy for prostate cancer, your risk of breast cancer is increased.
- **Family history of breast cancer.** If you have a close family member with breast cancer, you have a greater chance of developing the disease.

development of the testicles. As a result, men with this syndrome produce lower levels of certain male hormones (androgens) and more female hormones (estrogens).

- **Liver disease.** Certain conditions, such as cirrhosis of the liver, can reduce male hormones and increase female hormones, increasing your risk of breast cancer.
- **Obesity.** Obesity is associated with higher levels of estrogen in the body, which increases the risk of male breast cancer.
- **Testicle disease or surgery.** Having inflamed testicles (orchitis) or surgery to remove a testicle (orchiectomy) can increase your risk of male breast cancer.

Cancer of Unknown Primary Types

Cancer of unknown primary (CUP) is a disease that has metastasized (spread) from another part of the body. The place where it began, also called the primary site, is unknown. CUP make up about 2% to 5% of cancers diagnosed in the United States. As better diagnostic tests are being developed they are becoming less common.

As doctors examine CUPs more closely under a microscope, they usually decide the cancer belongs in one of the following categories:

Adenocarcinomas: About six of every 10 cancer of unknown primary cases are adenocarcinomas, meaning they began in gland cells. Most frequently, the primary sites are the lung, pancreas, breast, prostate, stomach, liver or colon.
Poorly differentiated carcinoma: Cancer cells are present, but they do not have enough detail for doctors to decide the type of cancer. Around 10% of these CUP cases are found to be lymphoma, melanoma or sarcoma.
Squamous cell cancer: The cells are flat, similar to cells on the skin or linings of some organs.
Poorly differentiated malignant neoplasm: Cells are definitely cancer, but they are so abnormal it cannot be determined what type of cell or part of the body they began in. Sometimes they are lymphomas, sarcomas or melanomas.
Neuroendocrine carcinoma: This type of CUP begins in the neuroendocrine system, making the cells like nerve cells and hormone-making cells. They are scattered in organs including the esophagus, stomach, pancreas, intestines and lungs.

Because the primary site of many cancer of unknown primary cases is never found, it is difficult to say what causes them. In the cases in which the primary site is determined, possible risk factors are based on that type of cancer.

- Smoking tobacco is a risk factor in cancers of the pancreas, lungs, kidney, throat, larynx and esophagus. More than half of people with CUP have used tobacco.

- Too much sun exposure causes some melanomas.

However, it has not been proven that any of these factors make a person more likely to develop cancer of unknown primary.

How AI Plays a Role in Diagnosing Breast Cancer

One of the most important things that can be done in detecting breast cancer early is having a mammogram and performing routine self check breast exams for symptoms and lumps in addition to one's annual check- up with their OB/GYN.

Breast cancer is still prevalent because most insurance companies don't want to cover the cost of mammograms if there is no proof that performing mammograms at an earlier age will detect breast cancer any earlier. In other words, for every 1,000 mammograms done, what percentage will detect breast cancer at an earlier age? That is why the recommended age of getting a mammogram now is back to over the age of 50.

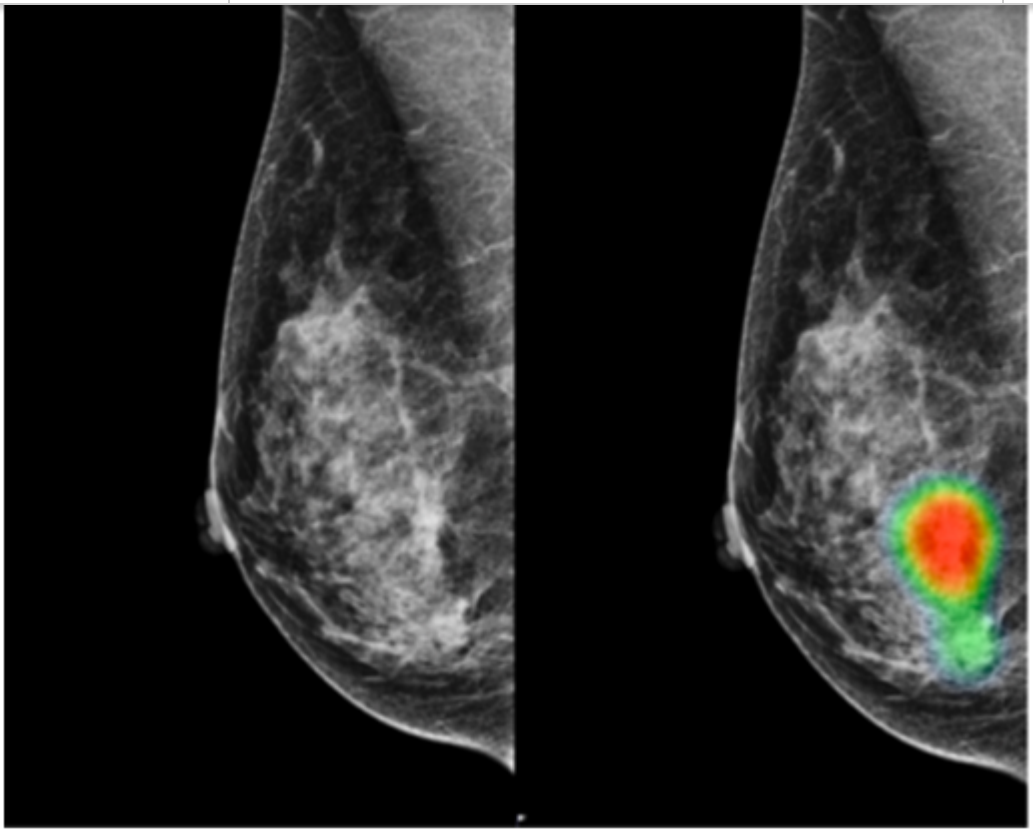
The United States Preventive Services Task Force (USPSTF) recommends that women who are 50 to 74 years old and are at average risk for breast cancer get a mammogram every two years. Women who are 40 to 49 years old should talk to their doctor or other health care professional about when to start and how often to get a mammogram. Women should weigh the benefits and risks of screening tests when deciding whether to begin getting mammograms before age 50.

40-49 years old, mammograms were yearly. Then in October of 2015, the guidelines started to restrict the age of when women could get a mammogram and today, it is 50 years and older every two years. This seems to be going backwards and not forwards. And one size does not fit all.

One of the reasons breast cancer is hard to detect in women are those women who have dense breast. Radiologist can't tell whether the dense image is cancer or dense tissue from a mammogram image thus resulting in further imaging test to rule out or rule in breast cancer.

Brian Dontchos, MD, Constance Lehman, MD, PhD, and colleagues at Massachusetts General Hospital trained and tested their machine learning model using a convolutional neural network they fed around 59,000 random 2D mammograms from around 40,000 women.

Their findings suggest that artificial intelligence can help head off unwarranted additional imaging, increase consistency among a practice's readers and help each radiologist better estimate true cancer risk. "[O]ur deep learning model reduces the proportion of screening mammograms categorized as dense and could reduce unnecessary supplemental imaging and better inform traditional risk models that rely on breast density to estimate breast cancer risk," Dontchos et al. comment in their discussion. "More widespread use of our deep learning model should be considered as this tool could supply more consistent information to patients and help healthcare systems more appropriately use limited supplemental screening and risk assessment resources."



Mammograms of a 49-year-old woman with invasive lobular carcinoma on the right-side breast. A small mass with micro-calcifications on the right-side breast was detected correctly by AI with an abnormality score of 96%. This case was recalled by 7 out of 14 radiologists (4 breast radiologists and 3 general radiologists) initially (without AI) and all 14 radiologists recalled this case correctly with the assistance of AI.

Computer-aided detection (CAD) boosted by AI has often proven superior to traditional CAD over the past decade, yet the “new way” has been slow adoption in breast cancer diagnosis due to a high cost of entry combined with knotty ethical and legal concerns.

Researchers as Columbia University researchers reviewed the literature on AI in mammography and found 10 key findings in five categories:

Comparison of traditional CAD and CAD based in convolutional neural networks (CNNs)

1. When compared to conventional CAD for digital mammography, CNN-assisted CAD has shown a reduction in false positives, improved sensitivity and nearly a 7% increase in area under the curve (AUC).
2. Because CNN-CAD systems have lower false positive rates than traditional CAD systems, they may be used to reduce recall rates. In some cases, the recall rate has been reduced by 10 to 20% due to a greater ability to distinguish benign images

AI as an assistive tool

3. When used as an assistive tool for human readers for digital mammography, the AUC of readers was statistically significantly higher with AI support than without it. With AI support, AUCs ranged from 0.797 to 0.89. Without AI support, these AUCs ranged from 0.769 to 0.87.
4. In two of these studies, sensitivity also significantly increased with the use of deep learning. In one study, reading time did not differ when AI support was used. In another, reading time decreased with the use of AI.

Standalone comparison to radiologists

5. In some studies, standalone deep learning software statistically significantly outperformed readers. When AUCs for AI programs were obtained in these studies, they ranged from 0.876 to 0.940, when compared with readers' AUCs, which ranged from 0.778 to 0.81.
6. However, in two out of the three studies where AI outperformed readers, the gold standard used was the radiologists' interpretation. In other studies, standalone deep learning was found to have a similar performance when compared to radiologists.

Deep learning for reducing interval cancer rate

7. AI programs can be used retrospectively to re-assess … cancers that were correctly marked by CAD as high-risk. In 2019, Hinton et al. showed an increase in AUC for the detection of interval cancer from 0.65 to 0.82 for full-field digital mammography when using AI. In 2021, Lang et al. and Graewingholt et al. showed that deep learning for digital mammography resulted in a 19.3% reduction in interval cancer and had a sensitivity of 48% for identifying interval cancers, respectively.
8. [I]n the study conducted by Lang et al., two breast radiologists classified prior mammograms with interval cancers as either true negative, minimal signs or false negative. This type of classification also occurred by radiologists in the study conducted by Graewingholt et al. Hence, one limitation of both studies is that observer bias may have falsely elevated the number of lesions determined by the radiologists to be "false negatives," which may have inflated the rate of interval cancer detection by the AI software.

Triage screening mammograms

9. For digital mammography and DBT, many studies have shown that an AI system can assist with identifying normal mammograms as cancer free, with Yi et al. indicating that deep learning can discard 53% of normal images, which were all found to be

10. In addition to reducing radiologist workload and costs related to screening, AI programs can reduce the number of false positives by identifying normal mammograms as negative. This is particularly helpful when the rate of recall is high, such as in the USA, because a reduction in false positives will reduce the number of benign exams that are recalled.

Academic researchers at China's Guangzhou University, along with industry researchers in the U.S. and China, found that combining AI models with reads from breast radiologists of mixed experience levels can help health systems consistently diagnose malignant architectural distortion on mammography. They conducted a retrospective review of mammograms acquired and interpreted over a six-year period at the university's affiliated medical center.

In introducing their findings, Daniel Q. Chen, Bo Liu and colleagues name breast architectural distortion as "the most difficult type of tumor to detect and the most commonly missed abnormality due to its inherent subtlety and varying attributes."

Comparing the performances of unaided radiologists with AI-aided peers at finding the malignancies, and of AI ensembles alone, the team recorded the following results:

1. Combining AI with a junior radiologist brought a specificity of 72.7% and sensitivity of 91.7%. These scores represented significant improvements over AI alone and radiologist alone.
2. The cumulative results of these and other comparison "underscore the potential of using deep learning methods to enhance the overall accuracy of pretest mammography for malignant architectural distortion,"
3. The "large gap" in the diagnostic acumen of radiologists across the many regions of China, suggesting the implications of the study extend beyond architectural distortion patients:

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Closing Thoughts

When Artificial Intelligence (AI) was first introduced to the healthcare field, many people were skeptical thinking that AI would take their jobs away. Today, we know that AI or machine learning is only as good as the person who programmed or wrote the algorithm and that AI is just as it states, machine learning. At first AI wasn't very accurate but as those who developed the algorithms, corrected the AI, it became better and more accurate.

AI has many advantages in healthcare as discussed above:

1. It is more accurate as the human mind can't process the amount of data a computer can and human error doesn't factor in with AI. It is always learning to become better.
2. It frees up more time for the radiologist as they don't have to read mammograms that are deemed negative with a high interval of confidence and focus on the images that are suspicious or inconclusive.
3. Some hospitals are already using AI to read pap smears that are deemed negative and highlights pap smears that needs a pathologist expertise.
4. Healthcare professionals will always be needed for mammograms, pap smears and any other tests that need their expertise.
5. AI is more consistent with results as parameters are always the same while inexperienced healthcare professionals may miss things their more tenure colleagues won't.
6. AI should make life easier overall.

AI is not perfect and can be subject to computer glitches or error for whatever reason. One can't write a software program and forget about it. Like most things, it requires maintenance in making sure that the software is working properly to what is expected.

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Should you have any questions or need of assistance with your business due diligence, determining your product's value proposition, target product profile and economic value of your product for reimbursement, feel free to contact me at 781-935-1462 or regina@biomarketinginsight.com.
