Imagion Biosystems, Ltd.

The Case for Non-Invasive and Earlier Detection of Cancer

The Role of Molecular Imaging

October 2022

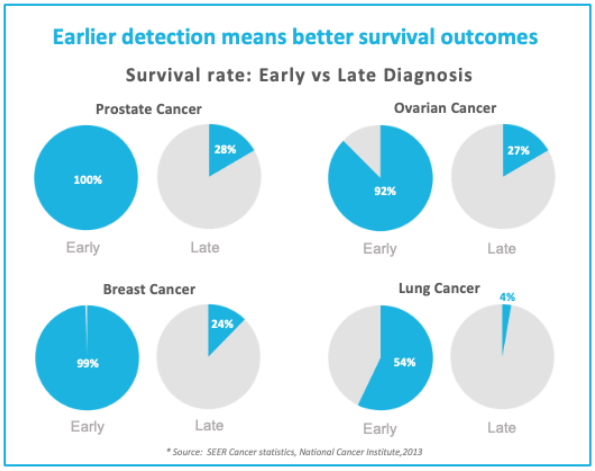
Non-Invasive and Earlier Detection of Cancer

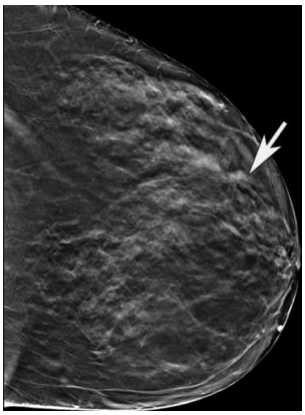
Overview

Imagion Biosystems is developing a new generation of molecular imaging technology for earlier non-invasive detection of cancer. Improvements in medical imaging technologies over the last 50 years have largely focused on improving sensitivity and image resolution but still largely remain limited to identifying "regions of interest". Though newer PET tracers aim to provide improved specificity, safety concerns related to the exposure of patients to radioactivity remain. The company's MagSense® technology is a new molecular imaging modality that uses targeted bio-safe magnetic nanoparticles to tag the cancer and locate the tumor. By using targeted nanoparticles, detection is highly specific differentiating cancer cells from benign growths and making it possible to detect smaller tumors than conventional imaging techniques that rely on anatomical characteristics. This combination of features has the potential to revolutionize how cancer is detected and treated.

Medical Need

"*Early detection of many diseases, particularly cancers, is key to successful treatment. However, traditional diagnostic and imaging techniques cannot detect tumors in early development stages and have limited ability in differentiating benign and malignant lesions.*" [1] Most cancers are largely asymptomatic. As a result, they grow undetected until large enough (tens or hundreds of millions of cells) to be detectable by X-rays, ultrasound, or MRI, or until they begin to cause identifiable symptoms. As a result, conventional cancer treatment does not start until a cancer has already progressed. The SEER Cancer Statistics graphic shown here illustrates the consequences of late detection. The graphs show that when cancer is detected at an early stage, survival for most cancers is good, but when detected at late stage, survival rates are poor.





Mammograms are a commonly used imaging method to screen for breast cancer. For a trained radiologist the bright spot highlighted by the arrow in the image at left is identifiable as an abnormality. But what is it? Is it a fibrotic mass or cancer? Over the past few decades imaging technologies have made significant improvements in image resolution and quality. And more recently artificial intelligence and machine learning are making advances in image analysis. As a result, we are seeing better sensitivity and an improvement in the ability for trained professionals to interpret disease or health conditions even for small lesions like that shown here. But despite these advances, to know for certain what the abnormality is requires a biopsy. And while obtaining a biopsy for breast cancer is no picnic for the patient, imagine the complications if the suspicious lesion is in the brain, the prostate, or internal organs like the ovaries or pancreas?

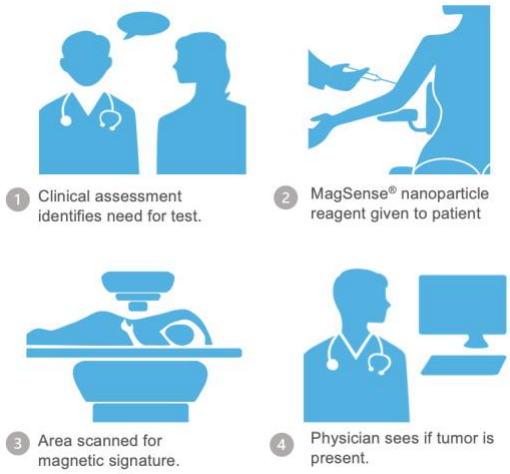
Cancer is a cellular phenomenon, but conventional imaging technology cannot identify or differentiate specific

[1] 2015 ACS Publications – Chem Reviews, Nanoparticles in Medicine

types of cells. Herein lies the mismatch with conventional imaging – current technologies only allow us to find "abnormalities" or "suspicious lesions", *i.e*. areas of tissue that don't look normal or are different than the surrounding "normal" tissue. This then requires the patient to undergo surgical or biopsy procedures to confirm if the suspect tissue is cancer. Many lives are shattered or lost because we can't diagnose cancer until it is big enough to be identified as suspicious and able to be biopsied.

The Era of Molecular Imaging

At Imagion Biosystems we believe the solution isn't just better image resolution but transforming imaging from identifying a "region of interest" to detecting molecular signatures of abnormalities and specific cancer cells. Our MagSense® molecular imaging agents are comprised of bio-safe magnetic nanoparticles with cancer-targeting molecules that provide the specificity of detection. When the MagSense® molecular imaging agent is given to a patient, for example as a simple intravenous injection, the tiny magnetic nanoparticles circulate with the normal flow of blood. If cancer cells are present, the nanoparticles attach themselves only to the targeted cancer cells and act as a magnetic beacon, detectable by magnetic imaging systems.



Product Pipeline

Our MagSense® molecular imaging agent for detecting HER2 metastatic breast cancer is the clinical phase of development and we have a R&D pipeline for other indications including prostate cancer, ovarian cancer, and brain cancer.

Breast Cancer

Breast cancer is the second leading cause of cancer related deaths in women and the second most common cancer diagnosed in women. Following diagnosis of the primary tumor, cancer staging is usually undertaken prior to treatment to determine if the cancer has metastasized. This often requires a lymph node biopsy where cells are taken from lymph nodes, or whole nodes for examination by a pathologist. More than 50% of patients are node negative which means that more than half of breast cancer patients undergo an invasive biopsy procedure unnecessarily. A non-invasive molecular imaging test could eliminate the unnecessary biopsies and the resulting costs and morbidities for many breast cancer patients.

Prostate Cancer

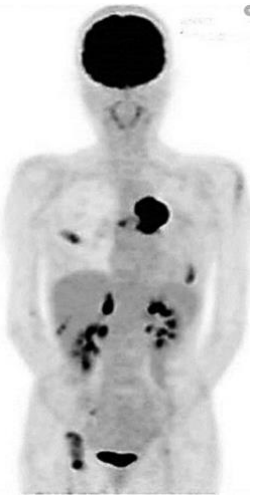
Prostate cancer is the second most frequent form of cancer found in men with approximately 1 in 7 men being diagnosed with prostate cancer during their lifetime. Prostate cancer is typically identified through routine screening with PSA blood-based testing. However, the PSA test is not diagnostic with only 25% of men with elevated PSA being positive for cancer. Core needle biopsies are typically done for men with elevated PSA with more than 1 million biopsies done in the U.S. alone. Since the biopsy procedure is both expensive and painful replacing the biopsy with a simple *in vivo* MagSense® test would be of significant benefit, reducing risk, cost, and pain for the patient.

Ovarian Cancer

Only about 20% of ovarian cancers are found at an early stage because ovarian cancer is largely asymptomatic and today's screening tools are not specific or sensitive enough to detect ovarian cancer at early stages. By the time a tumor is detected by ultrasound it is usually large (millions of cells) and late stage. Clinical data suggest that detection of ovarian cancer at an earlier stage leads to improved 5-year survival rates (90% for stage 1 vs 39% for stage III patients). A MagSense® imaging agent able to specifically detect an ovarian tumor at its earliest stages would significantly impact patient lives compared to today's "watchful waiting" by ultrasound.

Competitive Advantages

There are multiple imaging technologies in use today. MRI, ultrasound and mammography are the most frequently used in cancer diagnosis, with MRI offering the best image resolution. However, none provide the specificity of molecular imaging. Positron Emission Tomography (PET imaging) has been working in this direction since it first paired use of a radioactive tracer with a glucose molecule (FDG-PET). There are, however, three drawbacks to this approach. Firstly, PET scans have poor resolution so the patient may have both a PET scan and a CT (PET/CT) to overlay the location of the PET tracer with the anatomical image from the CT but adding cost. Secondly, both the PET tracer and the CT are radioactivity-based techniques exposing the patient to ionizing radiation. And thirdly, because the FDG tracer is not specific to cancer but to areas of high metabolic activity it goes everywhere – the brain, areas of inflammation etc. and so finding the "area of interest" amongst all the background accumulation can be challenging (see example at right). Recent advances in PET imaging are now pairing radio tracers with more specific biomarkers, like PSMA-PET for detecting prostate cancer cells. This is a welcome advance and is moving from functional imaging to true molecular imaging – where a targeting molecule ensures the specificity of the detected lesion. Unfortunately, the problems of poor resolution and use of radioactivity are still present with PET imaging.



Business Strategy

The MagSense® molecular imaging agents should command a premium reimbursement because they provide diagnostic imaging results and reduce other costs like biopsies. We expect to partner with leading imaging industry strategic partners to commercialize our high gross margin molecular imaging technologies.