Innovations in Cancer Diagnosis and Treatment: What’s on the Horizon

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Innovations in Cancer Diagnosis and Treatment
What’s on the Horizon

- An enormous amount of **time**, **energy**, and $$$ is being spent on innovations in detection and treatment of cancer.

- Some are already here, some… right on the horizon,

- Some have many years to reach fruition, and some will fail ….
Future of Cancer Diagnosis

• Much of the research in detection of cancer can be divided into two areas:

  – **Liquid biopsies** - A test that enables the diagnosis or analysis of tumor using only a blood or fluid sample rather than a solid tissue biopsy

  – **Artificial intelligence** - The simulation of human intelligence processes by machines, especially computers, such as:
    • Learning
    • Reasoning
    • Visual perception
    • Speech recognition
Liquid Biopsy

Tumour

Dying cancer cell

Blood sample

Needle biopsy

Circulating DNA
Liquid Biopsy

- Liquid biopsies typically detect:
  - Circulating tumor cells (CTCs)
  - Circulating tumor DNA (ct DNA)
  - Proteins shed by tumors

- Some types of liquid biopsies are not new.
  - fine needle aspirations
  - CTC identification in metastatic breast cancer
  - flow cytometry
  - CSF (cerebral spinal fluid)

- Some liquid biopsies complement tissue biopsies by detecting unique molecular characteristics to help determine which treatments are most likely to work for that patient.
Liquid Biopsy Tests - diagnosis non invasive

- **Guardant 360** - commercially available now, but not FDA approved yet
  - Blood test complements traditional lung biopsy to determine best treatment option for NSCLC.
  - May be better than traditional lung biopsies in identifying biomarkers.
  - Can identify recurrences

- **FoundationOne Liquid**
  - Detects ct DNA. Use to complement solid tissue results or when tissue is not ideal
  - Solid tumors including lung, breast, colon and others
  - 2 tubes of blood.

- New liquid biopsies are being developed to detect cancer early, before they can be seen or cause symptoms.

- **23 and Me**
  - At home saliva test
  - BRCA 1/BRCA 2 test for breast cancer
  - Detects 3 out of > 1000 know BRCA mutations
Liquid Biopsy Tests- diagnosis

- **Cancer Seek** - developed by Johns Hopkins University and first published in Science in January 2018. This blood test screens for 9 common cancers.
  - simultaneously evaluating levels of 8 cancer proteins and the presence of cancer gene mutations from ct DNA.
  - Best at detecting ovarian and liver cancers (98% success rate), worst in breast (33% success rate for stage 1 breast cancer).
  - Investigators envision that Cancer Seek will eventually cost less than $500.
  - Larger studies underway

- **Grail** - blood test in development that can find 12 cancers including Stage 1-3 solid tumors; colon, ER negative breast cancer, lung, head & neck, liver, ovarian, pancreas, myeloma and lymphomas.

- **Israel Institute of Technology and an International Consortium** - using breathalyzer to identify 17 different diseases, both malignant and benign (such as lung, kidney ca, Parkinsons, MS to name a few)
Some liquid biopsies being developed to monitor response to treatment.

- **Tgen (Translational Genomic Research Institute) and the Mayo Clinic** - Developing a liquid biopsy (TARDIS) to identify residual breast cancer after curative chemo
  - More sensitive than radiology
  - May prevent under/over treatment.

Other initiatives in development:
- Blood test to identify glioblastomas.
- Blood test to detect ovarian cancer up to 2 years earlier than current approaches.
- Urine tests to:
  - detect bladder, ovary and perhaps other cancers
  - monitor response to treatment
  - can be done at home
## Liquid Biopsy

<table>
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<th><strong>Pros</strong></th>
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<tbody>
<tr>
<td>• Non invasive</td>
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<tr>
<td>• Less expensive</td>
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<tr>
<td>• Requires less resources</td>
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<tr>
<td>• Faster</td>
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<tr>
<td>• Can be performed repeatedly</td>
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<tr>
<td>• Multiple applications: diagnosis at early stage, late stage, can help</td>
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<td>determine treatment, and monitor response of treatment</td>
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<table>
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<th><strong>Cons</strong></th>
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<tr>
<td>• What to do once a cancer is diagnosed?</td>
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<td>• Sometimes the treatment may be worse than living with a cancer that</td>
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<td>is not immediately life threatening.</td>
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<td>• Some cancers may be very slow growing, ex-prostate ca.</td>
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<td>• May not be as reliable as tissue</td>
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Artificial intelligence (AI) is being used in radiology.

• New breast ultrasound uses algorithms to make recommendations about whether a breast abnormality is benign or cancerous.

• How is this done? The program was fed 9,000 breast lesion images read by radiologists along with different characteristics noted. Each lesion was then biopsied. The system learned which characteristics were associated with positive biopsies.

• This ultrasound is commercially available in parts of Europe, the Middle East and Korea and was approved by our FDA in 2017.
Cancer Detection

MRI scans

- May take 15 - 60 minutes to perform – takes time to capture all the data needed to make a usable image

- Using AI may be possible to capture less data so the scan can be run much faster while still preserving or even enhancing the images
Artificial Intelligence

AI may complement liquid biopsy. According to a May 31, 2019 report:

- Thrive- partnering with Geisinger Health Plan (similar to Kaiser) and Johns Hopkins University to enroll 10,000 patients in a study pairing the Cancer Seek liquid biopsy test with a machine learning engine.
- Study will enable test to improve with each person screened.
- Test is designed to be integrated into routine medical care alongside existing cancer screening tools such as colonoscopy.
AI guided pathology

- Distinguishing between breast atypia and breast in situ disease is very challenging and subjective—which may lead to misdiagnosis.

- In testing, AI guided pathology did a better job than experienced pathologists.

- Tests are ongoing.
AI in Pathology

• Tissue diagnosis involves cutting tissue samples by hand, placing each between 2 pieces of glass and studying it under a microscope. The process largely unchanged in 150 years. A human can typically process about 12 samples per hour.
• A new robotic microscope can cut 1000 slices per hour while simultaneously scanning an image into a 3D tissue model.
• The 3D model is sent to pathologists who explore and translate the findings
Future of Cancer Treatment

Individualized Cancer Care using
Combination therapies
Cancer vaccines
Cancer cell genetics
Biosimilar drugs
Targeted Therapies

How do Targeted Therapies work?

• Target specific proteins on the cancer cell that control growth and development
  – Monoclonal antibodies
    • Block a specific target on the outside of cancer cells or area around the cancer. Covers the cancer cells like a blanket, block or turn off chemical signals that tell the cell to grow and divide.
    • Can introduce chemotherapy directly to cancer cells.
  – Small-molecule drugs
    • Stops the multiplication and spread of cancer cells.
      – Angiogenesis inhibitors- keeps tissue around the tumor from making blood vessels that “feed” the tumor
  – Well known targeted therapies
    • Herceptin
    • Avastin
    • Opdivo
    • Tarceva
Targeted Therapies


Targeted Therapies

Pros

• Less toxic than traditional chemotherapy because only cancer cells are “targeted”.

• Normal cells are not affected by therapy.

• Side effects of some targeted therapies have been linked to better patient outcomes.

Cons

• Side effects-
  – Diarrhea
  – Liver problems - hepatitis and elevated liver enzymes.
  – Skin problems (acneiform rash, dry skin, nail changes, hair depigmentation)
  – Blood clotting and wound healing
  – High blood pressure
  – Gastrointestinal perforation (a rare side effect of some targeted therapies)

• Effects of therapy may take longer to appreciate.
Targeted Therapies

Studies and Clinical Trails

- Locally advanced pancreatic cancer- Chemotherapy, radiation and Adavosertib (protein inhibitor).
- Glioblastoma- BKM-120 (protein inhibitor) with and without Multiple Sclerosis drug teriflunomide
- AML- FLT3 inhibitors like midostaurin, gilteritinib and crenolanib
Immunotherapy

• Many types of Immunotherapy, all stimulate an immune response in the patient’s body.
  – Checkpoint inhibitors- PD-1 and CTLA-4 proteins that prevent normal cells from being attacked. Cancer cells use the proteins to stop normal death. These drugs are now being combined to attack both proteins.
  – CD24- “Don’t eat me” signal- type of checkpoint inhibitor that allows cancer cells to avoid being attacked by white blood cells. Ovarian and triple-negative breast cancers may be well suited for CD24 inhibitor therapy.
  – ACR T-cell- patient’s T cells are harvested and altered to have chimeric antigen receptors that will help them to attach to leukemia cells and destroy them. NHCI is 1 of 2 programs offering CAR-T for AML in Georgia. Myeloma, CLL and Lymphoma currently in clinical trial.
  – Monoclonal antibodies- discussed in targeted therapies
  – Necroptosis- normal form of cell death in which the cell swells and explodes. A virus is used to deliver the genes undergoing necroptosis into tumors that in turn sparks an immune response.
  – Combination of immunotherapies to assist in immune-fatigue.
• **HPV vaccine.** The vaccine protects against the Human Papillomavirus (HPV).
  – Cervical, vaginal, and vulvar cancer
  – Anal cancer
  – Genital warts
  – Oral cancer not yet approved by the FDA.
  – Newly approved for up to age 45.

• **Hepatitis B vaccine.** This vaccine prevents hepatitis B virus (HBV) infection. Long-lasting infection with HBV can cause liver cancer.
Vaccines

New therapies, studies and clinical trials

• Prostate- uses patient’s white blood cells that are exposed to prostate cancer cell’s protein and then reintroduced to the patient via IV.
• Lymphoma- tumor is injected with a stimulate to recruit immune cells, tumor is treated with low dose radiation then reinjected to stimulate to activate immune cells that then go throughout the body to identify other tumors.
• Triple-negative Breast- personalized polyepitope DNA taken from patients will then be reinjected via IV as naked plasmid DNA vaccines.
• Solid Tumors- personalized peptide (amino acid) vaccine combined with adjuvant Poly-ICLC to boost immune response to peptides in tumor cells.
Oncolytic Virus Therapy

- Historically, some cancer patients found to go into temporary remission after a viral infection.

- Considered **Immunotherapy**- virus invades cancer cells, causing the cells to “burst” killing the cancer cells and releasing cancer antigens that in turn simulates immune response.
  - Can be viruses in natural state or genetically modified.
  - Most are injections given directly into tumor.
  - Can enhance effects of subsequent treatment.
Oncolytic Virus Therapy

T-VEC

- currently only FDA approved oncolytic therapy for Melanoma.

- Genetically modified herpes simplex virus that will less likely infect healthy cells and cause cancer cells to produce immune-stimulating proteins.

Doctor: I've got some bad news  
Me: lay it on me gently  
Doctor: ok, knock knock  
Me: who's there  
Doctor: herpes

:/
Oncolytic Virus Therapy

New studies highlight efforts to expand the number of cancer types treated with oncolytic virus therapies as well as the methods of delivery.

- **Poliovirus**
  - PVS-RIPO with chemotherapy- Clinical trial that will target glioblastoma tumors by crossing the blood brain barrier that traditional chemotherapy is not able to do effectively.
  - CRI CLIP- Clinical trial for triple-negative breast cancer
  - CRI- providing funding for clinical trials for advanced appendiceal, colorectal and ovarian cancers

- **Maraba (Sand Fly virus)**
  - clinical trial for triple-negative breast cancer- virus is sensitizing agent for immunotherapy
Biosimilar Drugs

- Derived from living organisms, such as yeast, bacteria, plant or animal cells.
- Drugs that are very similar, but not identical to the original biological drug. There cannot be any “clinically meaningful differences”.
- Biosimilar drugs are not generic drugs that can have the same active ingredients.
- The introduction of biosimilar drugs should lower the costs of treatment for patients.
Radiation Therapies

Radiation therapy for metastasis

- Whole brain radiation clinical trial for brain mets that avoided the hippocampus along with memantine protects cognitive function versus those that received standard whole brain radiation.
- Bone metastases clinical trial showed that a single high dose radiation was more effective than a multiple low dose regimen.
- Renal and bladder cancer metastases clinical trial- immunotherapy vs immunotherapy plus radiation.
- NSCLC Lung cancer metastases that has stopped responding to chemotherapy clinical trail - immunotherapy vs immunotherapy plus radiation.
- Stage T1 Bladder cancer post TURBT clinical trail- radiation along with radiosensitizing chemotherapy protocol.
Future of In-Patient Healthcare

Advent Health Command Center, Orlando Campus
Future of In-Patient Healthcare

Advent Health Command Center, Orlando Campus

- Network of 9 Central Florida hospitals.
- Wall to wall screens track every patient in real time, updated every 3-5 seconds.
- Patient information populated by 20 AI apps- 600,000 messages daily.
- Goals:
  - Reduce ER wait times
  - Reduce inpatient bed time
  - Reduce time to treatment
Conclusions

• Liquid biopsies and Artificial Intelligence will enhance cancer diagnosis now and in the future with earlier detection, greater accuracy and specificity for treatment options.

• The old ways of one-size-fits-all style of surgery, chemotherapy and radiation is no longer in the patient’s best interest. Innovations in genetic mapping and cell structure allow for a menagerie of treatment options.