New Imaging Techniques in Diagnosing Cancer

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Presentation Overview

- Cancer
  - Brief overview of cancer and related issues
- History of Diagnostic Imaging
- New Imaging Techniques
  - MRSI (Magnetic Resonance Spectroscopy)
  - Combinational Techniques
  - SPIO (Super Paramagnetic Iron Oxide)
- Conclusions
Cancer

- Cancer is a group of diseases which cells are aggressive, invasive, and metastatic.

- Nearly all types are caused by abnormalities of genetic material.

- Two abnormalities are: cancer-promoting and tumor-suppressing.
Tumors

- A tumor is an abnormal growth or mass of tissue.
- The abnormalities interfere with the cell’s ability to regulate cell division.
- Combinations of genetic abnormalities may cause a breakdown of the cell cycle.
Cell Cycle and Mitosis

- Tumor formation is caused by deregulation of the cell. Restriction point is compromised and cells undergo mitosis uncontrollably.
Lymphatic System

What does it do?
- Lymph = interstitial fluid in the lymphatic system.
- Not closed, and has no central pump
- Three functions
  - Removal of excess fluids from body tissues
  - Production of immune cells
  - Absorption of fatty acids
Lymph Nodes

- Filters or traps for foreign particles.
- Contain white blood cells.
- Lymph flows only in one direction.
- Cancerous nodes feel enlarged, firm, nontender, and fixed to underlying structures.
Metastasis

- Definition: The spread of disease from one part of the body to another, can occur via lymphatic vessels.
- All malignant tumors eventually metastasize
- Cancer cells may travel through blood or lymph to establish new tumors.
- Thus, secondary tumor sites can be predicted if the primary site is known.
TNM Staging

- The stage of cancer describes how much the cancer has spread.
- Uses roman numerals to describe the degree of staging.
- T (I – IV) staging involves the size of a tumor, and the direct extent of the primary tumor.
- N (0 - III) staging describe the degree of spread to regional lymph nodes.
- M (0 - I) is the presence of metastasis
History of Diagnostic Imaging

- Rudolf Virchow (1825–1902)
  - Cited as first to recognize Leukemia
  - Referred to as the “Father of Pathology”
  - *Omnis cellula e cellula* (“Every cell originates from an existing cell like it”)
  - Virchow’s Node, the supra-clavicular node is the one of the earliest sign of gastrointestinal cancer.
X-ray Imaging (1895-1900)

- 1895 – X-rays first discovered by German physicist Wilhelm Conrad Roentgen. He also produced the first x-ray picture of the body (his wife's hand) in 1895.
- 1900 – Chest X-rays, widespread use of the chest x-ray made early detection of tuberculosis (which was the most common cause of death) a reality.
X-ray Imaging (1906-1912)

- 1906 – X-ray contrast medium. First contrast filled image of the renal system (kidneys).
- 1912 - *Barium sulfate* introduction of as contrast agent for gastro-intestinal diagnosis.

An x-ray system from the pioneering days. Patients still had to hold the cassettes themselves.
Nuclear Medicine (1950’s)

- Nuclear Medicine studies (also called radionuclide scanning) were first done in the 1950s using special gamma cameras. Nuclear medicine studies require the introduction of very low-level radioactive chemicals into the body. These radionuclides are taken up by the organs in the body and then emit faint radiation signals which are measured or detected by the gamma camera.

- Applied imaging to the kidneys, heart, and skeletal system.
Ultrasound Imaging (1960)

- Developed to look at the abdomen and kidneys, fetal baby, carotid blood vessels and heart.
- The principals of sonar were applied to diagnostic imaging.
- Placing a transducer, against the skin of the patient near the region of interest.
- This transducer produces a stream of inaudible, high frequency sound waves which penetrate into the body and bounce off the organs inside.
- The transducer detects sound waves as they bounce off or echo back.
Computed Tomography (CT)

- Also called Computed Axial Tomography (CAT)
- Invented in 1972 by Godfrey Hounsfield
- Hounsfield used gamma rays (later changed to x-rays) to create detailed cross sectional images
- Originally took hours to take one slice of image data
- 1989 – Spiral CT was invented allowing fast volume imaging
Magnetic Resonance Imaging

● 1950’s MR principles first investigated
● Developed by Paul Lauterbur
● 1980 - First MRI of a brain performed
● 1993 – Open MRI systems developed

During magnetic resonance imaging (MRI), a narrow tube moves the patient through a tunnel-like structure. Inside the structure, radio waves pass through a magnetic field around the patient, creating a 3-D image of the internal structures.
Positron Emission Tomography

- 1985 – Developed at the University of California
- Utilizes nuclear medicine and gamma rays to create image
- Best method for actually diagnosing cancer
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What is MRSI?
Magnetic Resonance Spectroscopy Imaging, more specifically in this case its Proton MR Spectroscopy.

What does MRSI do?
Its method is to perform an MRI and at the same time perform Proton (\(^1\text{H}\)) Spectroscopy of the tissue.
**Principles of MRSI**

During the MRI and radio frequency (rf), a map of proton signal intensity by location is produced.

Additional, the signal from each proton has a different frequency known as its chemical shift.

MRSI measures the chemical shift property to produce a map of signal intensity versus frequency and spatial location.
Imaging Techniques - MRSI

- **MRSI and Prostate Cancer**
  
  The relevant metabolic peaks are choline and citrate. They have distinct frequencies on the chemical shift map so their peaks can be seen readily.

  Choline is a normal chemical found in the cell membrane (used for cell signaling) and is found at large levels within tumors.

  Creatine is an organic acid that supplies energy to cells.
Imaging Techniques - MRSI

- Prostate Cancer and MRSI
  Choline levels are high in prostate cancer and creatine is very low.

  The map of shift frequency versus spatial location allows oncologists to find clusters within tumor that are particularly aggressive.

  Aggressive areas can be treated with high doses of radiation, relative to other, less aggressive areas of the tumor.
Imaging Techniques - MRSI

- Chemical Shift Map versus Spatial Location
Imaging Techniques - MRSI

- Prostate Cancer Treatment with MRSI
  Without knowing the internal composition with the Spectroscopy higher doses of radiation would have to be applied to the entire prostate.

  This is a risk because increasing radiation uniformly increases chance of treatment mortality.

  Perform gradient dosage (ie. Applying different levels of radiation to certain locations within a tumor) to destroy high risk areas.
Imaging Techniques - MRSI

- Tumors areas: Aggressive areas
Imaging Techniques - MRSI

- MRSI - Prospect of eliminating biopsy
  MRSI provides a way to find tumors with MR imaging as well as composition.

  Historically breast and prostate cancer have a biopsy performed if there is a suspicious mass found in the image.

  Knowing the chemical composition such as the choline:citrate ratio can reduce the need for biopsies to prove cancerous tumors as well as reduce false-negative biopsies.
MRSI and Imaging

During MRSI, the large tissue water and lipid signals must be actively suppressed in order to detect the metabolites in the prostate, which are present in much lower concentrations.

The three-dimensional MRSI data are acquired using water and lipid suppression. This is a double spin echo (SE) sequence.

The MRI/MRSI grid is done by relaying the spectroscopic grid on a T2 weighted sequence.
Advantages

- Can diagnose, localize, and plan treatment to prostate and lesser degree breast cancer.

- MRI/MRSI are readily accessible to public.

- Requires no contrasting agent, makes a very feasible cost.

- High sensitivity and specify.

Disadvantages

- Limited to certain metabolites with distinct chemical shift.

- After therapy, prostate has low T2 intensity, so repeating images is of no use.

- Abnormal metabolic levels interfere with interpretation.
Imaging Techniques - Combinational

● Purpose
  - To incorporate aspects of different techniques in one image.

● Examples
  - PET/CT
  - SPECT/CT

● PET/CT
  - Anatomical advantages of CT scanning
  - Tissue differentiation properties of PET scanning
  - Especially important for treatment
Imaging Techniques – PET/CT

- CT Scanning
  - Provides an anatomical image based on the density of tissues.
  - Used to help guide biopsy procedures
  - Helps the planning stages of radiotherapy and surgery
  - Determines whether the cancer is responding to treatment
PET Scanning
- Provides images of blood flow, or other biochemical functions.
- Common functions include detecting glucose metabolism or rapid activity changes.
- Useful in determining the extent of spread of certain cancers.
Case Study #1 – The Skeletal System

- 117 patients participated in this study
- The purpose was to show PET/CT’s superiority in diagnosing cancer in bones over simply PET or CT alone.
- Used fluorine18 Fluorodeoxyglucose as the radioactive substance for the PET scans
Imaging Techniques – PET/CT

- Comparison of PET, CT and fusion images.
Imaging Techniques – PET/CT

- Tables 1, 2, and 3 demonstrate the percentages of accurate diagnoses of tumor, nodal, and metastases stages respectively.

<table>
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<tr>
<th>Modality</th>
<th>Accuracy (%)*</th>
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<tbody>
<tr>
<td>Conventional imaging</td>
<td>94 (65/69)†</td>
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<tr>
<td>PET</td>
<td>80 (55/69)†‡§</td>
</tr>
<tr>
<td>PET/CT</td>
<td>96 (66/69)‡</td>
</tr>
<tr>
<td>Combined PET/CT and conventional imaging</td>
<td>99 (68/69)§</td>
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<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)*</th>
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<td>Conventional imaging</td>
<td>53 (9/17)</td>
<td>97 (97/100)</td>
<td>75 (9/12)</td>
<td>92 (97/105)</td>
<td>91 (106/117)†</td>
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<td>PET</td>
<td>72 (13/18)</td>
<td>96 (96/100)</td>
<td>76 (13/17)</td>
<td>95 (96/101)</td>
<td>93 (109/117)</td>
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<td>PET/CT</td>
<td>88 (14/16)</td>
<td>97 (99/101)</td>
<td>82 (14/17)</td>
<td>98 (98/100)</td>
<td>96 (112/117)</td>
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<tr>
<td>Combined PET/CT and conventional imaging</td>
<td>88 (14/16)</td>
<td>99 (100/101)</td>
<td>93 (14/15)</td>
<td>98 (100/102)</td>
<td>97 (114/117)†</td>
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<td>Conventional imaging</td>
<td>65 (32/49)†‡§</td>
<td>90 (61/68)</td>
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<td>PET</td>
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<td>PET/CT</td>
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<td>88 (46/52)</td>
<td>97 (63/65)</td>
<td>93 (109/117)†</td>
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Imaging Techniques – PET/CT

- Case Study #2 – Brown Fat
Imaging Techniques – PET/CT

- Case Study #3 – Colon Cancer
  Even when PET clearly shows a malignant tumor, improved localization on PET/CT can assist in patient management. The patient in this case had a history of colon cancer.
Imaging Techniques – PET/CT

- **Advantages**
  - Ability to see both the anatomy and physiology in one picture.
  - Overall Decreased Scan time
  - Better Identification of inflammatory regions
  - Improved Localization for Biopsy or Radiotherapy

- **Disadvantages**
  - Minor Limitations in CT Portion
  - Likewise less clear differentiation in
  - Increased Radiation
  - Technical Difficulties (With improvements these will decrease)
  - Potential Claustrophobia
Imaging Techniques - SPIO

● What is SPIO?
Super Paramagnetic Iron Oxide (SPIO) is an MRI contrast agent, meaning it will affect the contrast of (MR) Imaging to provide different information than a standard MR image.

● Types of SPIO
There are two types of SPIO. Standard SPIO uses iron oxide particles with a mean diameter of 50nm+. The second is Ultra small SPIO, which vary in size a great extent but still much smaller mean diameter.
Imaging Techniques - SPIO

- What are SPIO particles made of?
  Ferrites composed of maghemite \((\text{Fe}_2\text{O}_3)\) and magnetite \((\text{Fe}_3\text{O}_4)\).

Metal ions occupy different positions in the crystalline lattice, resulting in a net spontaneous magnetic moment.
Biocompatibility of SPIO Injection
Good biocompatibility of liver uptake.
Normal livers may contain up to 0.2 mg of iron per gram of liver.
Also a human may contain up to 3500 mg.
Using SPIO for imaging purposes, a normal amount used is roughly 50 to 200mg.

Too much SPIO?
Chronic use is not recommended because iron toxicity develops after liver iron concentrations reach over 4mg per gram of liver. The SPIO will be concentrated in the liver and disperse through the body, so long concentration times could potentially develop into iron toxicity.
Imaging Techniques - SPIO

- **How does SPIO affect MR Imaging**
  The super paramagnetic properties of iron oxide particles induce strong magnetic field distortions around the particles. On T2*-weighted sequences, this effect generally results in marked, focal signal defects.

  The property used is called magnetic susceptibility which is used in mainly Gradient Echo Sequences (GRE)

- **Spin Echo (SE) versus Gradient Echo (GRE)**
  GRE providing lower SNR and spatial resolution than Spin Echo sequences (SE), T2*-weighted GRE sequences are more sensitive to our magnetic field distortions.
Imaging Techniques - SPIO

- SPIO and Liver Metastasis (LM)
  Liver metastasis can use SPIO imaging to detect cancerous tumors and metastasis. The primary way in which this works is because of cells in the liver called Kupffer cells, which are macrophages.

Since these cells are only found in healthy tissue, we expect to see signal decrease only in areas where SPIO particles were consumed by macrophages.
Imaging Techniques - SPIO

- SPIO and Liver Metastasis (LM) (cont’)
  The tumors, which are absent of such macrophages, end up showing a greater contrast between diseased tissue and healthy tissue.
Imaging Techniques - SPIO

- USPIO and lymph nodes
  Ultra small SPIO (USPIO) particles can detect lymph node metastasis. Macrophages can’t intake the regular SPIO like the Kupffer cells can.
Imaging Techniques - SPIO

- SPIO versus Portal Phase CT
Imaging Techniques - SPIO

- SPIO Compared to Other techniques

A - B - C - D
Imaging Techniques - SPIO

- **Advantages**
  - Small amount of iron can produce large results.
  - Studies of oncologists show SPIO is much more accurate than 16-Detector Row CT scan.
  - No other equipment other than MRI using standard MRI values.

- **Disadvantages**
  - Expensive to produce.
  - Lacks industrial process which adds to complexity and cost of making the specialized particles.
  - Small doses are fine, but chronic doses can produce iron toxicity.
Conclusion

- Diagnostic imaging has come a long way. Significant improvements have been made on many machines, and new techniques are arising to better locate cancer and give accurate spatial geometry with good quality.

Any Questions?
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