Agenda

• Our Patients Presentation.
• Current challenges in Imaging Modalities.
• What is Nanotechnology/Nanomedicine?
• Why Nano-material properties change?
• Nanotechnology Applications.
• Nano Applications in Diagnostic Imaging.
• Dangers behind using Nano.
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49 Year old Female, known to have osteoporosis presented to the clinic with intermittent constipation, nausea & vomiting.

She passed 2 kidney stones last year, she had a bone lesion 7 months ago in the right tibia that was diagnosed as osteitis fibrosa cystica.

No significant past medical or surgical illnesses, non smoker on vitamin D supplements & bisphosphonates.
Our Patient:
Physical Examination

- Patient is **lethargic** but not in pain or distress.
- Vitals are stable.
- Chest clear, bilateral air entry, no wheezing.
- CVS Normal S1+S2+0
- Abdomen soft lax, non tender & bowl sounds present.
- Some swelling at the mid portion of the right tibia
- No other significant findings
Our Patient:

Labs

- CBC: Normal
- U/E: Serum Ca+ 14.7 mg/dL (High)
- Urinary Ca+ >400mg (High)
- PTH: 107 (High)
Our Patient:
Investigation Plan

• Our Patient was diagnosed with primary hyperparathyroidism.

• We ordered a parathyroid Ultrasound & Nuclear scan to identify the culprit gland.
Our Patient:

Right Inferior Parathyroid Adenoma on Ultrasound

- Dist 0.474 cm
- Dist 0.550 cm
- Dist 0.774 cm
Our Patient:
Right Inferior Parathyroid Adenoma on Ultrasound

- Strip Muscles
- Rt Jugular Vein
- Inferior Rt Parathyroid
- Parts of arterial vessels

Our Patient: Right Inferior Parathyroid Adenoma on Ultrasound

Saif Aljabab 2011
Gillian Lieberman, MD
Our Patient:

Color Doppler showing avascular adenoma at same location

Dist 0.945 cm
Our Patient:

Color Doppler showing avascular adenoma at same location

Inferior Rt Parathyroid

Dist 0.945 cm
Our Patient:

Rt Inferior Adenoma on Sestamibi Scan

Courtesy of: Kevin Donohoe, MD

PACS, BIDMC
Our Patient:
Rt Inferior Adenoma on Sestamibi Scan

Parotid Gland

Submandibular Glands

Thyroid Gland

Heart

Mouth

Nose

Inferior Rt Parathyroid

Our Patient:
Rt Inferior Adenoma on Sestamibi Scan

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Rt Inferior Adenoma on Sestamibi Scan

Inferior Rt Parathyroid

Courtesy of: Kevin Donohoe, MD

PACS, BIDMC

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Our Patient:

Differential Diagnosis

• Differential Diagnosis of a mass in the parathyroid that may give symptoms of primary hyperparathyroidism:
  
  • Parathyroid Adenoma.
  • Parathyroid Hyperplasia.
  • Parathyroid Carcinoma.
Medical Management: Estrogen if patient is post-menopause to prevent osteoporosis / Bisphosphonates to control hypercalcaemia.

Surgical Management: Surgical Removal of the culprit gland while monitoring Parathyroid hormone levels.

Our patient went for surgical parathyroidectomy.
• **Surgery:** The adenoma was sitting immediately below the lower lobe as predicted. The upper left parathyroid was enlarged as well, parathyroid hormone level post-op was **23** after both were removed.

• **Pathology:**
  - **Right lower parathyroid (A):** Cellular parathyroid tissue, consistent with parathyroid adenoma.
  - **Upper left parathyroid (B):** Cellular parathyroid tissue consistent with parathyroid adenoma
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Challenges we faced with our patient

• In our patient we missed the left upper adenoma, in most cases the Sestamibi scan will show the presence & location of an adenoma, confirmed by ultrasound results.

• However, current imaging modalities miss the location of an adenoma in few cases, difficulty in localization escalates as we try to identify a carcinoma & its possible metastasis.
The Need to Improve

- Mixed results can happen, where ultrasounds identify a different location of an adenoma than a Sestamibi scan, in some cases the surgeon identifies a third location.

- Currently PET, SPECT, MRI, CT & U/S are the most modalities of imaging used to diagnose, localize, stage & follow up with cancer patients.
The Need to Improve

• These modalities are quite useful clinically but are not perfect, and its accuracy falls down even more when trying to detect micro metastasis.

• This raises the issue that we need to find new more improved ways to detect tumors accurately.
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NanoTechnology has a potential role in detecting tumors more accurately
What is 100,000 times thinner than a strand of hair & 20 times tougher than steel?

A Carbon Nano-Tube

$(1 \times 10^{-9} \text{ m})$

[Image: A Carbon Nano-Tube, magnification x500, scale 50μm, 1.00kV, 6mm]

http://www.nsf.gov/od/lpa/news/03/pr03147.htm
What is Nano Technology?

• Its not biology, physics or chemistry its all sciences that deal with such a small scale.

• Best Definition: “Encompasses the common unifying concepts & physical laws that prevail in the Nano scale “ www.nanoscience-europe.org
What is Nano-Medicine?

- Nanomedicine may be defined as the monitoring, repair, construction and control of human biological systems at the molecular level, using engineered Nanodevices and Nanostructures.
Humans have unwittingly employed nanotechnology for thousands of years.

Damascus Steel, a type of steel used in sword making from 300 BC – 1700 AD was discovered to contain nanowires & nano carbontubes.

Http://www.wired.com –
http://steelguru.com/article/details/NiI%3D/Damascus_Sword.html
Nanotechnology in Nature

• When it comes to Nature, they are the king of nanotechnology.

A flagella structure is a complexity of Nano rotors, motors, tubes & arms that work perfectly together, many of which we still try to decipher how they work.

http://micro.magnet.fsu.edu/cells/ciliaandflagella/ciliaandflagella.html
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Physical Properties change

• When everyday material is converted to a Nano scale they start to act in unpredictable ways.

• Many of the physical properties of substances we know change at this scale, as if projecting the tablet of elements into several dimensions.

• Understanding how they start to work and what physical properties change can be tricky.
Theory Behind Properties Changes:

1- Quantum Confinement

- When items are turned this small, the movement space of its electrons becomes much more limited than it prefers, this increases its kinetic energy, gaining it more speed.
Theory Behind Properties Changes:

2- Surface to Volume Ratio

• Things this small have much more outside than inside, most of the material may be surface and very little can be volume.
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Nanotechnology Applications

• Over 600 products in the market currently use nanotechnology, from golf clubs to Nanotex clothing, cosmetics, paints to Solar energy cells, water filters.

Nanotex clothing are resistant to liquid stains, you can spill what you want on it.

Applications in Medicine

• Radiation Therapy, drug delivery systems, regenerative medicine, biosensors for detecting salmonella in food products, tissue engineering, dendrimers in gene therapy.
• Opens the era of personalized medicine.
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Nano Application in Diagnostic Imaging

- Currently using Nano-particles is the mainstay of research in enhancing diagnostic imaging.

- There are 4 major advantages that these Nano-particles give to improve imaging in comparison to other techniques like Molecular imaging.
1- Larger surface allows for a multi functional ability in interacting with more molecular agents/particles.

2- A Stronger Amplifier of signals that can be detected outside the body which may help detect micro metastasis.

3- Multi modality competence, in that it can enhance signaling of several imaging modalities.

4- Both diagnostic & therapeutic (theranostic) potential.
Gold(Au) Nano-particles are a versatile material whose natural resistance to surface oxidation makes it ideal for a wide-range of research applications.

These particles are being used now in research to detect colorectal cancer, specially flat lesions that are difficult to see on colonoscopy, the gold nanoparticles can be detected using a Raman spectroscopy.
Examples of Nano Diagnostic Imaging

http://www.fleetattorney.net/tag/colon-cancer/
Examples of Nano Diagnostic Imaging

- **Photo-Acoustic Imaging Nano-particles**, these particles are used in research to develop a new modality of detecting tumors.
- Light enters the body heating the particles enough to produce a sound -but not enough to harm tissue- that can be detected by an external source.
- Example of such particles that can be used are Carbon nanotubes & Gold nanoparticles modified to emit sounds.

Examples of Nano Diagnostic Imaging

• **Iron nanoparticles** which are iron oxide nanoparticles coated with dextran are another example of nanoparticles used in diagnostic imaging.

• These particles are mainly used to target lymph nodes for cancer spread detecting it with MRI.

• The particles are taken up by normal cells in the lymph node but not by cancer cells.

Examples of Nano Diagnostic Imaging

- Patients would first take an MRI, afterwards be injected with Iron nanoparticles then take another MRI image after 24 hours.

- Lymph nodes that take the nanoparticles will change color to black, cancer cells will stay bright.

MRI: Lymph node before & after injecting with Iron nanoparticles

http://www.prostate-cancer.org/pcricms/node/172

Figure 3. Spectrum of nodal signal intensity changes with magnetic nano-particles a-c. Normal lymph node in the left iliac region on (a) non-contrast MR and (b) 24 hours after intravenous administration of ferumoxtran-10 (arrow). Note the homogeneous decrease in signal intensity due to ferumoxtran-10 accumulation. (c) corresponding histology (10x objective). d-f: Non-enlarged iliac lymph node completely replaced by tumor (arrow). (d) conventional MR showing high signal intensity lymph node; (e) 24 hours after ferumoxtran-10 administration. Note that nodal signal intensity remains high. (f) corresponding histology. g-i: Micro-metastases in retroperitoneal node. (g) MRI showing high signal intensity lymph node; (h) ferumoxtran-10 enhanced MRI demonstrating two hyperintense foci (arrows) within the node corresponding to 2 mm metastases. (i) Corresponding histology confirms the presence of adeno-carcinoma within the node. Reprinted with permission from New England Journal of Medicine.
Examples of Nano Diagnostic Imaging

• **Gold nanoshelled microcapsules** are a combination of electrostatic gold nanoparticle depositions onto microcapsules and a surface seeding method which results in the formation of gold nanoshells.

• This nano/microcomposite is able to operate as a theranostic agent for both contrast-enhanced ultrasonic imaging (diagnostic) and photo hyperthermia (therapeutic), and thus holds a great potential for photothermal therapy in cancer treatment.

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With the development of nanomaterial's, environmental & health concerns are mounting about exposure & its safety regulations.

For example respirator filter masks may not protect against Nano particles being inhaled!! They can pass through normal human protective barriers and reach the deepest structures within our tissue reacting with them.
Dangers Behind Using Nano

- A research model on rats which made them inhale carbon nanotubes showed that their lungs did react to the nanoparticles and inflammation was noted, most of the inflammation did clear out with time.

- Currently there is lack in regulation of nano production on companies due to the very little data available on its toxicity.
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References

- http://www.upToDate.com/
- Beth Isreal Deconess Hospital Careweb Portal.
« It’s a Small World
After All »
Thank You