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Asociacion Latinoamericana De Sociedades De Biologia y Medicina Nuclear (ALASBIMN)
Asia Regional Cooperative Council for Nuclear Medicine (ARCCNM)
Association of Nuclear Medicine Physicians of India (ANMPI)
Asian School of Nuclear Medicine (ASNM)
Society of Nuclear Medicine, India (SNMI)
INFECTION IMAGING

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IMAGING INFECTION

- Major cause of mortality and morbidity:
  - developing countries, globally.
- Tuberculosis and multi-drug resistant bacteria are increasing
  - diagnostic and therapeutic challenges.
- The issue has gained global importance because of
  - a growing geriatric and immuno-compromised population that are extremely vulnerable to infection
  - resurgence of resistant tuberculosis in the Western world and
  - continuing primacy of infective disorders in the tropical and developing countries.
INFECTION LOCALIZATION

• Prompt localization of infection sites
• Appropriate Therapeutic measures
• Major advances in the field of treatment
  – Newer antimicrobial therapies are increasingly available
• Early Diagnosis is still the major problem
• Infection still remains a major cause of patient morbidity and mortality.
A tissue injury due to infection initiates a series of physiochemical events in the damaged tissue resulting in enhancement of:
- tissue perfusion
- vascular permeability
- transduction of plasma proteins (opsonins, antibodies, complement)
- influx of leucocytes

Involving a variety of complex mediators, both vasoactive and chemotactic.

A nuclear scan provides information on pathophysiological and biochemical changes underlying an infection before the appearance of focal changes in:
- tissue density
- Composition
- necrosis or
- abscess formation
INDICATIONS FOR RADIONUCLIDE IMAGING FOR INFECTION

- Opportunistic Infection
  - Immuno-compromised patients
- Fever of Unknown Origin (FUO)
- Postoperative Infection
- Cardiovascular & CNS Infections
- Bone Infection
  - Hematogenous osteomyelitis
  - Diabetes,
  - Following orthopedic procedures for fracture or joint replacement,

- Early Diagnosis
- Extent of the disease
- Treatment Response
OVERVIEW OF RADIONUCLIDE INFECTION IMAGING

- Radiopharmaceuticals used
- Advantages & Disadvantages
- Clinical Indications
- Recent Advances
- Future Perspectives
PROPERTIES OF AN IDEAL INFECTION IMAGING RPS….

- Ready availability
- Ease of preparation
- Low cost
- Non-toxic
- No side effects
- No immune response
- High sensitive
- High specific
- Good target to non-target ratio
- Rapid uptake at the sites of infection
- Ability to differentiate bacterial infection from sterile inflammation
## INFECTION IMAGING
### RADIOPHARMACEUTICALS

<table>
<thead>
<tr>
<th>No</th>
<th>Radiopharmaceutical</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tc-99m MDP</td>
<td>Increased bone memetabolism, Chemisorption, Blood flow</td>
</tr>
<tr>
<td>2</td>
<td>Tc-99m Leukocytes (HMPAO)</td>
<td>Migration of activated leukocytes (diapedesis &amp; Chemotaxis)</td>
</tr>
<tr>
<td>3</td>
<td>Tc-99m Ciprofloxacin</td>
<td>Binding to DNA-Gyrase enzyme present in living bacteria</td>
</tr>
<tr>
<td>4</td>
<td>Tc-99m Nanocolloids</td>
<td>Increased vascularity/ Uptake in activated endothelial cells</td>
</tr>
<tr>
<td>5</td>
<td>Tc-99m Granulocyte Ab</td>
<td>Binding to surface antigens (NCA-90) of granulocytes</td>
</tr>
<tr>
<td>6</td>
<td>Tc-99m/ In-111 Hlg</td>
<td>Antigen binding/ Increased capillary permeability</td>
</tr>
<tr>
<td>7</td>
<td>Tc-99m/ In-111 Liposomes</td>
<td>Increased vascular permeability</td>
</tr>
<tr>
<td>8</td>
<td>Tc-99m Colloids</td>
<td>RES uptake</td>
</tr>
<tr>
<td>9</td>
<td>Tc-99m DTPA</td>
<td>Capillary Permeability</td>
</tr>
<tr>
<td>10</td>
<td>Tc-99m Fanolesomab</td>
<td>Immunoglobulin that binds to CD15 receptors present on the leukocytes</td>
</tr>
<tr>
<td>11</td>
<td>Ga-67 Citrate</td>
<td>Transferrin &amp; Lactoferrin receptor binding</td>
</tr>
<tr>
<td>12</td>
<td>In-111 Leukocyte</td>
<td>Migration of activated leukocytes</td>
</tr>
<tr>
<td>13</td>
<td>In-111 platelets</td>
<td>Incorporated into infected thrombus</td>
</tr>
<tr>
<td>14</td>
<td>In-111 Antimyosin Ab</td>
<td>Exposed myosin molecules</td>
</tr>
<tr>
<td>15</td>
<td>In-111 Octreotide</td>
<td>Expressed preferentially on granulocytes, activated lympho</td>
</tr>
<tr>
<td>16</td>
<td>F-18 FDG</td>
<td>Increased glucose uptake by activated leukocytes</td>
</tr>
</tbody>
</table>
MOST IDEAL INFECTION IMAGING AGENT!!

• The very fact that we have such a large number of agents, it is clear that not a single one of them can be considered ideal

• Some may be good for specific infections

• Appropriate choice of radiopharmaceutical may yield optimum diagnostic yield
PROPER USE OF THESE RPS REQUIRES.....

• Good understanding of the methods, strengths & weaknesses

• Bio-distribution, which depends on:-
  – Chemical properties, stability, purity
  – Pathological status of the subject,
  – Drug interference

• Clinical application:
  – When to use what?
  – In what combination
COMMONLY USED RADIOPHARMACEUTICALS

1. Tc-99m MDP
2. Tc-99m HMPAO Leukocytes
3. Tc-99m Granulocyte Ab
4. Tc-99m Fanolisomab
5. In-111 Leukocytes
6. F-18 FDG
Tc-99m Diphosphonates

- Skeletal imaging agent of choice
- Extremely sensitive for bony abnormality
- Uptake of Tc-99m MDP depends on:
  - Blood flow and the rate of new bone formation.
- Non-specific
- When performed in conjunction with a Three-Phase protocol, adds specificity
- Increasing diagnostic yield when combined with other radionuclide imaging procedures
Tc-99m MDP
THREE PHASE BONE SCAN IN OSTEOMYELITIS

Perfusion

Blood Pool

Delayed Scan
THREE PHASE BONE SCAN IN BONE TB

Pre Anti-tubercular Therapy

X-ray- ?Normal

Post Anti-tubercular Therapy

X-ray- Abnormal
Hip Joint Prosthesis (Tc-99m MDP)

Normal
Hip Joint Prosthesis (Tc-99m MDP)

Normal

Loosening

Infection
2. Tc-99m/In-111 Leukocytes

- Radio-labelling of inflammatory cell that migrate.
- Significant milestone
- Established and approved methods:
  - Make use of the Lipophilic compounds In-111 oxyquinoline and 99mTc-HMPAO.
- Procedure takes about 2–3 hours, Approximately 40 mL of whole blood
- All the cellular components of the blood can be labeled
- Separation of the leukocytes from the erythrocytes and platelets
1. Initial intense pulmonary activity
2. Slow progress of activated leukocytes in pulmonary vascular bed
3. Delayed 4 and 24 hr images normally reveal activity in the liver, spleen and bone marrow
4. In case of In-111, 24 hrs study offers much better quality images to interpret
Tc-99m/In-111 Leukocytes

- Uptake is dependent on:
  - intact chemotaxis
  - number and types of cells labeled
  - cellular component of a particular inflammatory response.
- Total WBC count of at least 2,000/mm$^3$ for satisfactory images.
- Most useful in Neutrophil-mediated inflammatory processes (bacterial infections)
- Less useful for illnesses in which the predominant cellular response is other than neutrophilic, such as tuberculosis
Tc-99m HMPAO WBC INFECTION IMAGING
TC-99m HMPAO WBC SCAN - Sacral Osteomyelitis
Tc-99m HMPAO WBC in a patient with Pseudomonas bacteremia: Mandibular Osteomyelitis

Blood Pool  1 hour  4 hours  Mandible Spot View
### Advantages & Disadvantages

<table>
<thead>
<tr>
<th>Tc-99m HMPAO Leukocytes</th>
<th>In-111 Leukocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ideal energy for imaging</td>
<td>• Less than ideal photon energy</td>
</tr>
<tr>
<td>• High Photon flux</td>
<td>• Requires technical adjustment for this dual photo-peaks (174 and 247 keV)</td>
</tr>
<tr>
<td>• Normal biodistribution more variable</td>
<td>• Low photon flux</td>
</tr>
<tr>
<td>• Imaging starts a few hrs after i.v. injection</td>
<td>• Stable label</td>
</tr>
<tr>
<td>• Best suited for imaging acute inflammatory conditions</td>
<td>• Constant biodistribution</td>
</tr>
<tr>
<td>• In addition to the RES, the activity also in GU Tract, large bowel, blood pool, Gall bladder</td>
<td>• Good quality delayed 24 hrs images may be obtained</td>
</tr>
<tr>
<td>• Poor quality delayed 24 hrs image</td>
<td>• Best suited for imaging indolent infections more effectively, such as prosthetic joint infection, etc.</td>
</tr>
</tbody>
</table>
3. Ga-67 Citrate

- One of the oldest radiopharmaceuticals
- Initial Euphoria: “Magic Bullet”
- Non-specific uptake
- Cyclotron produced
- Emits 4 principal $\gamma$ rays (93, 184, 296, 388 keV)
- Factors governing Ga-67 uptake:
  - 90% of Ga-67 is in plasma
  - All are bound to transferrin
  - Increased blood flow & Increased vascular permeability

Increase delivery and accumulation of transferrin bound Ga-67 at inflammation foci
3. Gallium-67 Citrate

- Transferrin
- increased blood flow
- increased vascular membrane permeability
- binds to lactoferrin which is in high concentration in inflammatory foci
- transported bound to leucocytes
- direct uptake by certain bacteria and binding to siderophores

Ga-67 Citrate: Normal Distribution

Bone, Bone marrow, Liver, GU Tract, GI Tract, Soft tissue
Ga-67 Citrate Imaging for Infection

SPECIFIC USES OF Ga-67

- Immunocompromised pts.
- Highly sensitive for Pneumocystis Carinii infection
- Monitoring response
- Better than Tc-99m HMPAO WBC for detection of opportunistic infection (Most opportunistic infection do not incite neutrophilic response)
- Adjunct to bone scanning in osteomyelitis
- Helps in infection monitoring following antimicrobial therapy
  - Bone scan may remain positive even after effective treatment of infection
  - Ga-67 will become negative
- Useful in Head & Neck infections
Malignant Otitis Externa

- Diabetics and people whose immune systems are compromised by diseases or medications are particularly susceptible to malignant otitis externa.
- The infection spreads from the floor of the ear canal to the adjacent tissues and into the bones at the base of the skull. The bones may be damaged or destroyed by the resulting infection and inflammation.
- The infection may further spread and affect the cranial nerves, the brain, or other parts of the body.
- Early localization and treatment reduces morbidity.

Ga-67 SPECT/CT INFECTION IMAGING

Diabetes with right skull base osteomyelitis (Baseline)

Diabetes with right skull base osteomyelitis (Post-therapy)

NEWER RADIOPHARMACEUTICALS

PEPTIDES, ANTIGRANULOCYTE ANTIBODIES/ANTIBODY FRAGMENTS

**Murine monoclonal IgG1 (Granuloscint) (CISBio International)**
- Binds to nonspecific cross-reactive antigen-95 present on neutrophils. Studies generally become positive by 6 h after injection; delayed imaging at 24 h may increase lesion detection.

**Leukoscan (Sulesomab) (Immunomedics)**
- Antibody fragment of the IgG1 class that binds to normal cross-reactive antigen-90 present on leukocytes. Sensitivity and specificity of this agent range from 76% to 100% and from 67% to 100%, respectively.

**Fanolesomab (NeutroSpec)**
- Another antigranulocyte antibody, a monoclonal murine M class immunoglobulin that binds to cluster designation 15 (CD15) receptors present on leukocytes. Fanolesomab can be labeled quickly and easily with 99mTc-pertechnetate. In contrast to in vitro labeled leukocytes, there is no increased retention of activity in the lungs. Based on available data, the agent is safe, with little toxicity. No serious adverse events occurred among any of more than 400 patients enrolled in multicenter trials.


- (Adverse effects reported/Taken out of the market)
Recent Fracture, Surgical manipulation, Suspected Infection

Tc-99m MDP

Leuko Scan
PROBLEMS WITH CONVENTIONAL AGENTS

• By far the most commonly used radiopharmaceutical is Tc-99m HMPAO WBC
  – Highly sensitive
  – Non-specific
  – Expensive
  – Time consuming
  – Too much handling of blood elements
  – Elaborate infrastructure (sterile suite etc)
  – Not suitable for differentiating infective conditions from inflammatory ones.
  – Useful only in specific conditions
IDEAL PROPERTIES OF AN IDEAL INFECTION IMAGING RPS….

- Ready availability
- Ease of preparation
- Low cost
- Non-toxic
- No side effects
- No immune response
- High sensitive
- High specific
- Good target to non-target ratio
- Rapid uptake at the sites of infection
- Ability to differentiate bacterial infection from sterile inflammation
Tc-99m CIPROFLOXACIN

- Based on a synthetic 4-Fluroquinolone broad spectrum antibiotic Ciprofloxacin labeled with Tc-99m.
- First developed at St. Bartholomew’s Hospital, London (INFECTON)
- INFECTON imaging has been reported to be more specific in localizing bacterial infection than WBC imaging
CIPROFLOXACIN

• Ciprofloxacin is the generic international name for the synthetic antibiotic manufactured and sold by Bayer Pharmaceutical under the brand names Cipro® and Ciproxin® belonging to a group called fluoroquinolones.

• Ciprofloxacin is bactericidal

• Its mode of action depends on blocking of bacterial DNA replication:
Taken up by live bacteria……..

• This approach is based on the use of labelled antibiotics that can be specifically metabolised by different microorganisms.

• It is taken up by viable bacteria and it does not accumulate in non-bacterial inflammatory lesions.

• The labeled compound gets right into the bacterial DNA with the help of its ligand Ciprofloxacin, whose anti-bacterial action is mediated via binding to, and inhibition of bacterial DNA gyrase.
Tc-99m CIPROFLOXACIN: Ability to differentiate bacterial infection from sterile inflammation

• No handling of blood products
• **Taken up by live bacteria**
• Not taken up by non-infective inflammatory tissues
• Not dependent on patient’s WBC counts
• Reasonable cost
• Easy to prepare
First International Multicentre Study

- Sponsored by the IAEA
- Total No. = 879 patients
- Male = 493
- Female = 386
- Mean age = 49.3 yrs
- Range = 1-97 yrs

IAEA Multi-centre study
Results

Overall:

Sensitivity = 85.5%
Specificity = 82.3

Positive Predictive value = 92.3%
Negative Predictive value = 69.5%
# Sensitivity & Specificity of Infection in Imaging Sites of Infection

<table>
<thead>
<tr>
<th>Suspected Infection</th>
<th>Case Definition</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osteomyelitis</strong></td>
<td>Study Criteria (N=228)</td>
<td>90.5%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=73)</td>
<td>86.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>72.8%</td>
</tr>
<tr>
<td><strong>Orthopaedic Infection</strong></td>
<td>Study Criteria (N=194)</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=63)</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Tuberculosis</strong></td>
<td>Study Criteria (N=131)</td>
<td>79.5%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=52)</td>
<td>90.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76.9%</td>
</tr>
<tr>
<td><strong>Soft tissue</strong></td>
<td>Study Criteria (N=45)</td>
<td>82.4%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=18)</td>
<td>94.5%</td>
</tr>
<tr>
<td><strong>Abdominal</strong></td>
<td>Study Criteria (N=44)</td>
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<tr>
<td></td>
<td>Microbiology +ve cases (N=15)</td>
<td>93%</td>
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<tr>
<td><strong>Surgical Wounds</strong></td>
<td>Study Criteria (N=27)</td>
<td>81%</td>
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<tr>
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<td>Microbiology +ve cases (N=13)</td>
<td>85%</td>
</tr>
<tr>
<td><strong>Septic Arthritis</strong></td>
<td>Study Criteria (N=27)</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=7)</td>
<td>75%</td>
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<tr>
<td></td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Endocarditis</strong></td>
<td>Study Criteria (N=26)</td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td>Microbiology +ve cases (N=13)</td>
<td>62%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100%</td>
</tr>
</tbody>
</table>
Beyond IAEA

• Subsequent to the IAEA CRP
• Several countries have taken up the task of producing their own INFECTON
• Peru, India, Chile, Serbia etc.
• Indian researchers: Singh et al are the most active group in this field
• Brought up many improvements in the original IAEA kit
• Now it is available commercially as a single vial kit
Tc-99m CIPROFLOXACIN: Infection vs. Inflammation

Right humeral and Lumbar prostheses: Infection vs. Inflammation

Tc-99m WBC

Tc99m Infection
Left knee Prosthesis

X-Ray

Bone Scan

Tc-99m INFECTON

S.Aureus Infection of Femoral Component
Tc-99m INFECTON: Septic Arthritis
Multiple fractures of Tibia & Fibula

Osteomyelitis of tibia
Tc-99m INFECTON: Hip Prosthesis

Infection around the hip prosthesis
Tc-99m INFECTON scan in a patient of diabetes with osteomyelitis of right foot. Please note intense radiotracer uptake in the lesion.

- Diabetes mellitus is a major disease affecting millions of global population
- 10-15% of Diabetics would have foot complications
- Morbidity, disability and mortality
- Most commonly encountered complication: Mal perforans Ulcer which accounts for >90% of diabetic pedal osteomyelitis
- Other complication: Neuropathic Joint (Charcot’s joint)
- Radionuclide infection imaging helps in diagnosing superadded infection

STERILE ULCER VS. SUPERADDED INFECTION
Advantages of Tc-99m Ciprofloxacin

- Robustness of the technique
- Safe
- No side effect
- Lack of bone marrow uptake is an advantage
- This imaging approach to bacterial infection avoids blood taking and labelling of blood components such as white cells with the possibility of needle stick injury and viral transmission.
- It is applicable to the evaluation of infection in the immunosuppressed and neutropenic patients.
PET IN INFECTION & INFLAMMATION

- FDG PET Important diagnostic tool in cancer imaging based on the principle of localization of elevated glucose metabolism
- Inflammatory cells also use glucose as an energy source when they are activated by variety of stimuli as a result of infectious processes
- Furthermore, a variety of cytokines and growth factors, which are often elevated in infectious disorders, dramatically enhance glucose uptake by inflammatory cells
- Inflammation & Infection Can Also Result in Increased Levels of Glucose Transporters on Inflammatory Cells
Case-03-EJE

- A 32 years old male
- Right thigh mass lesion and right leg swelling
X-Ray Chest

Opacity in the right cardio-phrenic angle

Suspicious for malignancy
Contrast CT of lower extremity

* necrotic tumour in the anterior compartment of the right antero-lateral thigh. ? Metastatic ? Sarcoma

Contrast CT of Chest

* Right lung lower lobe mass inferior to the right lower lobe pulmonary vein, enlarged mediastinal nodes. Multiple liver lesions
PET/CT STUDY
PET/CT STUDY
PET-CT STUDY
PET-CT Findings:

- Intensely FDG avid soft tissue lesion with central area of necrosis at right thigh
- Multiple FDG avid hypermetabolic lesions in:
  - Nasopharynx (with necrotic mass)
  - B/L Level II, III Cervical Lymph Nodes
  - Multiple mediastinal LNs (Paratracheal, carinal, subcarinal)
  - Right hilar LNs
  - Bilateral lungs (Multiple pulmonary nodules), with a large speculated mass right lung lower lobe
  - Multiple Liver
  - Inguinal LNs
  - Bones
Differential Diagnosis

• Primary tumor in right thigh with extensive metastases
• Could be two primaries:
  – Soft tissue tumor
  – Primary lung cancer with metastases
• Infection
  – Granulomatous
  – Acute Bacterial
Final Diagnosis

• Bone Marrow Biopsy:
  – Extensive hematopoietic effacement by necrotizing granulomatous infiltration
• Right thigh swelling (true cut biopsy)
  – Necrotizing granuloma favoring Tuberculosis
• Left lateral pharyngeal wall biopsy:
  – Necrotizing granuloma (Tuberculosis)
• AFB Culture (Tissue and Blood - right thigh)
  – Mycobacterium Tuberculosis Complex
Well....... 

• Some may call it “non-specific imaging” as far as cancer imaging is concerned
• Others may take full advantage of the technology to manage infection
• PET and PET/CT are now being introduced more and more in the Developing world
• The role of PET in diagnostic imaging will be further re-defined in due course as we gain more and more experience and
ADVANTAGES OF PET IMAGING IN INFECTION

• Simpler procedure
• Avoids the complexities of WBC labelling
  – handling
  – potential cross contamination of blood samples
  – High radiation dose
  – Time to imaging diagnosis
• Recent work on F-18 FDG labeled WBC PET/CT combines the high sensitivity of PET with high specificity of labelled WBC and appears to be highly promising (Dumarey N, et al. J Nucl Med 2006; 47: 625-632).
AV Prosthesis Infection

F-18 FDG PET

F-18 FDG PET
PET/CT in a case of FUO

CT

F-18 FDG PET/CT

Final Diagnosis: Pancreatitis
Ca. Lung: Post chemotherapy Opportunistic Chest Infection

Pre-Chemo

Post-Chemo
Treatment Response in Tuberculosis

Pre-Treatment

Post-Treatment
INFECTION IMAGING: CONCLUSIONS

• Nuclear Medicine Plays an important role

• Tc-99m MDP, Ga-67 Citrate, In-111 Oxine and Tc-99m HMPAO labelled WBCs are extremely useful

• Tc-99m HMPAO WBC most widely used, but the technique has several limitations

• Many a time a single test may not be enough

• A mix of two or more tests may yield more diagnostic information (e.g., a bone scan + WBC scan, etc)
INFECTION IMAGING: CONCLUSIONS

• Intelligent and selective use necessary to achieve effective results

• Studies are underway to ascertain whether some of these radiopharmaceuticals can be used through serial imaging (conversion of positive to negative image) to monitor the response to and the requirement for antimicrobial therapy.

• Infection imaging may play an important role in rationalising antimicrobial prescribing practices and thus contribute to the fight against antibiotic resistant bacteria.

• FDG PET/CT and FDG-WBC PET/CT are still at an early stage, but may prove to be useful in the future
Thank you very much
Specific Applications in Bone Infection
RADIONUCLIDE IMAGING IN BONE AND JOINT INFECTIONS

- Osteomyelitis
  - Acute Pyogenic
  - Tuberculosis of bones
  - Post-operative infection
  - Post-traumatic (Infection associated with fracture)
- Prosthesis Function:
  - Infection
  - Loosening
- Infection in Diabetic patients
  - Diabetic foot
  - Base of the skull infection
<table>
<thead>
<tr>
<th>Venue</th>
<th>Dates</th>
<th>Chairman, Local Organizing Committee</th>
<th>Chairman, International Organizing Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cartagena de indias</td>
<td>November 2009</td>
<td>Dr. Patricia Bernal T</td>
<td>Prof. A.K. Padhy</td>
</tr>
</tbody>
</table>

**ICRT-2009**  
3rd International Conference on Radiopharmaceutical Therapy
CIPROFLOXACIN

- Ciprofloxacin is a first generation fluoroquinolone antibiotic which is active against both gram-positive and gram-negative bacteria.
- It inhibits the “A” sub-unit of the DNA gyrase enzyme
- And thus interferes with the strand cutting and resealing function during DNA replication
CIPROFLOXACIN

- Intravenous injection
- Widely distributed in the body
- Excreted via the kidneys
- Microbiological activity is mediated by inactivation of bacterial DNA gyrase
  - Results in retention of the agent at sites of active bacterial infection
  - That forms the basis of imaging
Progress of “INFECTON”

- Initial IAEA kit used formamidine sulphonate acid as the reducing agent that had to be boiled before use (Unwanted, but necessary step)
- Later modified by using stannous tartrate reduction method (No boiling)
- Both - Two-vial kits for final preparation
- Most of the clinically used radiopharmaceuticals in nuclear medicine imaging are single-vial kits.
- Besides, significant amount of colloid formation upon reconstitution with Tc-99mO4-.
- Singh et al have come out with a single vial kit
- With high labeling efficiency and minimal colloid content.
- The colloid formation has been kept at the minimum by using physiologically acceptable excipients like sodium chloride, potassium chloride etc., to protect the interaction of Ciprofloxacin with stannous ions.
INFECTION LOCALIZATION

• Typical signs of infection and inflammation are useful in localizing the pathology at superficial sites.
• Extremely difficult in case of internal structures without the aid of imaging procedures.
• The role of radionuclide imaging in the evaluation of the patient suspected of harboring an infection varies with the situation. For example:
  – In the postoperative patient, radionuclide imaging is complementary to CT and is used to help differentiate postoperative changes from infection.
  – In the case of the painful joint replacement, in contrast, radionuclide studies are the primary diagnostic imaging modality for differentiating infection from other causes of prosthetic failure.
PET IN INFECTION & INFLAMMATION

In cancer patients:
• FDG accumulation in inflammatory or infectious tissues reduces specificity

In patients with suspected infection and no known cancer
• FDG PET may be extremely helpful in localization of infection

In difficult cases (Post surgery – Cancer vs Infection or inflammation)
• Kinetic analysis or serial PET imaging
Tc-99m CIPROFLOXACIN Imaging

- Highly diffusible molecule
- Taken up initially at sites of inflammation
- The uptake decreases as the blood level decreases
- Non-specific uptake fades at 4 hours compared to the 1-hour image and fades further or disappears at 24 hours
- What remains in the delayed image is due to uptake at infected sites