PET CT IMAGING IN INFECTION AND INFLAMMATION

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Infectious diseases account for more than 13 million deaths a year.

Over the next hour, 1,500 people will die from an infectious disease (50% under 5 years).

Most deaths from infectious disease occur in developing countries.

Mass population movements.
Health costs $bn

- Cancer: $895.2bn
- Heart Diseases: $343.9bn
- Lower Respiratory Infections (including Pneumonias): $125.8bn
- Cerebrovascular disease: $298.2bn
- Road Accidents: $204.4bn
- Infection: $92.8bn
- Cirrhosis of liver: $2.4bn
- Malaria: $24.8bn
- HIV/AIDS: $196.6bn
<table>
<thead>
<tr>
<th>World</th>
<th>Deaths in millions</th>
<th>% of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>7.25</td>
<td>12.8%</td>
</tr>
<tr>
<td>Stroke and other cerebrovascular disease</td>
<td>6.15</td>
<td>10.8%</td>
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<tr>
<td><strong>Lower respiratory infections</strong></td>
<td>3.46</td>
<td>6.1%</td>
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<tr>
<td><strong>Chronic obstructive pulmonary disease</strong></td>
<td>3.28</td>
<td>5.8%</td>
</tr>
<tr>
<td><strong>Diarrhoeal diseases</strong></td>
<td>2.46</td>
<td>4.3%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1.78</td>
<td>3.1%</td>
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<tr>
<td>Trachea, bronchus, lung cancers</td>
<td>1.39</td>
<td>2.4%</td>
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<tr>
<td><strong>Tuberculosis</strong></td>
<td><strong>1.34</strong></td>
<td><strong>2.4%</strong></td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.26</td>
<td>2.2%</td>
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<tr>
<td>Road traffic accidents</td>
<td>1.21</td>
<td>2.1%</td>
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</tbody>
</table>
90% death by 6 deadly infectious diseases

1. Pneumonia

2. Tuberculosis

3. Diarrhoeal diseases

4. Malaria

5. Measles

6. HIV/AIDS

Account for 50% of all premature deaths.
Nuclear Medicine Studies in European Market
Infection and Inflammation

Source: Medical Options – Survey 2012
INDICATIONS FOR NUCLEAR MEDICINE

- Fever of unknown origin
- Post-operative infection
- Osteomyelitis
- Granulomatous disease
- Fungal infections

Potential for Quality Research is Enormous
Radiopharmaceuticals

**On Table**

**CONVENTIONAL**

- 3 Phase bone scan
- Radiolabelled WBCs
- Ga-67

**PET Tracers**

- $^{18}$F & $^{18}$F-FDG
- Ga-68
- Hypoxia ($^{18}$F-fluoromisonidazole)
- Apoptosis ($^{18}$F-labeled annexin)
- Angiogenesis ($^{64}$Cu-DOTAPEG2 [c(RGDyK)])

**Current and previous tracers used**

- $^{18}$F-FDG
- $^{68}$Ga-Citrate
- $^{68}$Ga-Siderophores
- ImmunoPET
- WBC ($^{111}$In-oxyquinoline,$^{99m}$Tc-HMPAO)
- $^{67}$Ga Citrate and Nitrate
- $^{201}$Tl
- $^{99m}$Tc-IgG
- $^{99m}$Tc-Ubiquicidine
- $^{111}$In-HIG
- $^{99m}$Tc-Besilusomab/Sulesomab
OVERVIEW

• Respiratory System
  • Sarcoidosis
  • Sarcoid like reaction
  • Tuberculosis
  • Fungal
• Musculoskeletal System
• Cardiovascular system
• Vasculitis
• Nervous system
• Fever of unknown origin
SARCOIDOSIS
Sarcoid like reaction

Sarcoidosis is NOT
“All in my Head”

Sometimes it’s in my knees, nerves, eyes, liver, spleen, ankles, heart, spine, skin, lungs, lymph nodes, glands, bones...

(I could go on if you’d like.)
SARCOIDOSIS

• Sarcoidosis is a multisystem disease of unknown etiology that involves the formation of non-caseating granulomas.

• Initially there is nodal involvement and later there is involvement of the lung parenchyma.

• $^{18}$F-FDG PET-CT has better sensitivity (>90%) than $^{67}$Ga Scintigraphy (~81%)

• PET identifies 15% more disease sites than conventional imaging modalities.


No Large Prospective Trial
TUBERCULOSIS

TB Zumla , Lancet Volume 378, No. 9785, p57–72, 2 July 2011
Tuberculosis (TB) is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent. In 2011, 8.7 million people fell ill with TB and 1.4 million died from TB.

Over 95% of TB deaths occur in low- and middle-income countries, and it is among the top three causes of death for women aged 15 to 44.

In 2010, about 10 million orphan children.

Multi-drug resistant TB (MDR-TB) is present in virtually all countries surveyed.

Old disease – New threat: Hidden killer is MDR TB

London remains TB capital of Western Europe
Currently $^{18}$F-FDG PET has no major role in diagnosis of primary pulmonary TB.

$^{18}$F-FDG will play an important role in Extrapulmonary TB and Drug resistant TB

1. Prof Dragana Sobic Saranovic (lecture)
2. IAEA CRP E15021
   
   Use of $^{18}$F-FDG PET/CT for Imaging Extrapulmonary Tuberculosis Patients

Potential for Further Research
About 5,600 new HIV Infections a day in 2014
- About 66% are in Sub Saharan Africa
- Approximately 600 are children under 15 years of age
- About 5,000 are in adults aged 15yrs and older, of whom almost 48% are women & 30% are young (15-24yrs)
Lymphomatous lesions may improve while TB lesions develops

Warwick, Sathekge. Transfusion and Apheresis Science 2011
Viremic vs Aviremic patient

Mhlanga et al EJNMMI 2014
FUNGAL INFECTIONS

• Main challenge for clinical Haematologists.

• Immunocompromised appropriate adjustment of the therapeutic regimen.

• Chronic focal and disseminated fungal infections may persist long after completion of treatment and CT plays only a limited role in assessing therapeutic response that is further hampered by the complications associated with antifungal agents.

No Large Prospective Trial
26 yr Female with chronic cough after completion of therapy for Lymphoma

60 yr Male with blood tinged sputum after completion of therapy for Leukaemia
OSTEOMYELITIS

Conventional imaging is non-specific

- Active infection has to be differentiated from postoperative complications of reparative work.
- Artefacts associated with metallic implants further complicate diagnosis.
24 yr old M, with Osteomyelitis after tibial fracture from bike accident
Post-traumatic osteomyelitis


Sensitivity 94% Specificity 87% Accuracy 91%

- Axial skeleton
  - 88%, 100%, and 90%
  - 100%, 85%, and 91%

- Peripheral skeleton


$^{18}$F-FDG PET-CT was superior to $^{99m}$Tc–labelled antigranulocyte antibody scintigraphy for detecting chronic osteomyelitis in the axial skeleton.
DISCITIS

MRI MODIC CLASSIFICATION:

Degenerative changes on MRI

- Type 1 (Decreased signal intensity on T1-weighted and increased signal on T2-weighted images)

- Type 2 (Increased on T1-weighted and isointense or slightly increased signal on T2-weighted images).
METAL IMPLANTS

Conventional imaging modalities
- Limited after arthroplasty owing to the presence of metal artifacts.
- Feasible to image Titanium-based metal implants, the positioning of the patient and the variability of protheses are potential limitations
INFECTIVE ENDOCARDITIS

Systemic embolization is increased in patients with mobile vegetations of >1 cm. PET-CT can be of value in imaging such vegetations.

PERICARDITIS

- Myocardial tracer uptake limits role of FDG.
- Incidental findings
  - Patients with FUO

**Imaging Key:**
High Fat, Low Carb diet
VASCULITIS

Main value - Diagnosis of large vessel vasculitis

Sensitivity 77%-92%
Specificities 89%-100%

Giant cell arteritis
Takayasu arteritis

K.D.F. Lensen et al: Large-Vessel Vasculitis: Interobserver Agreement and Diagnostic Accuracy of 18F-FDG-PET/CT


No Large Prospective Trial
VASCULAR GRAFT INFECTION
CENTRAL NERVOUS SYSTEM INFECTIONS

**VIRAL:** Meningitis, various forms of Encephalitis

**BACTERIAL:** TB, Leprosy, Neurosyphilis, bacterial meningitis, Lyme disease

**FUNGAL:** Cryptococcal meningitis, Brain abscess, Spinal epidural infection

**PROTOZOAL:** Toxoplasmosis, Malaria, Primary amoebic meningoencephalitis

**PARANEOPLASTIC & AUTOIMMUNE DISORDERS**

- High background metabolic activity complicates the use of $^{18}$F-FDG PET-CT in imaging brain parenchyma.

- Most common indication remains “Limbic Encephalitis”
<table>
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<tr>
<th>Neuroimaging Before Neurologic Improvement</th>
<th>After Improvement</th>
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<tbody>
<tr>
<td><strong>MRI (FLAIR)</strong></td>
<td><strong>FDG-PET</strong></td>
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<tr>
<td>Patient 1</td>
<td></td>
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<td>Patient 2</td>
<td></td>
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<td>Patient 3</td>
<td></td>
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<td>Patient 5</td>
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No Large Prospective Trial
FEVER OF UNKNOWN ORIGIN

• $^{18}$F-FDG PET-CT replacing conventional scintigraphy, for imaging FUO.

• Causes:
  – Infectious disease (23.1%)
  – Non-infectious inflammatory disease (30.6%)
  – Malignancy (10.7%)
  – Other (12.4%)
  – Unknown (23.1%)

• Useful in 50% of cases (Range 16%–69%).

• Probability of reaching a diagnosis higher if $^{18}$F-FDG PET findings abnormal


SUMMARY

WE HAVE A LOT OF WORK TO DO

POTENTIAL FOR RESEARCH

INDICATIONS FOR $^{18}$F-FDG PET-CT

WELL ESTABLISHED

• Sarcoidosis
• Tuberculosis
• Osteomyelitis
• Endocarditis
• Vasculitis
• Vascular graft infections
• FUO

DEBATED

• Fungal infections
• Asbestosis
• Pericarditis
• Central nervous system infections
Thank You