Nuclear Medicine in HIV Update with FDG PET

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Outline

- Introduction
- Brief about general nuclear medicine
- FDG in HIV: Update & Potential

HIV/AIDS: EPIDEMIOLOGY

- Sub-Saharan Africa < 10% of the world's population, yet contains;
  - 90% of the paediatric cases
  - 68% of the adult cases
  - 76% of the global AIDS-related deaths

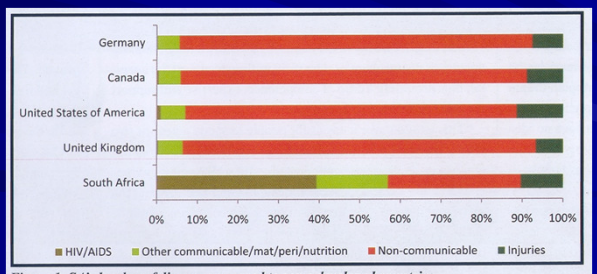


Figure 1: SA's burden of disease compared to some developed countries

Source: Econex calculations from WHO 2009 data*

HIV/AIDS: South Africa

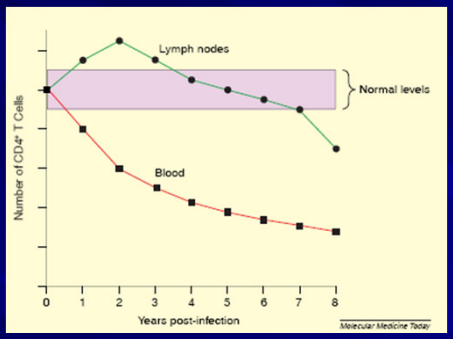
- 5.5 million of the 33.2 million
- > 1,400 new infections p/d ,
  - (~ to nearly one infection every minute)
- Average of 950 AIDS deaths
  - (~to one AIDS death every 90 seconds)
- Projections by 2015
  - Cumulative AIDS deaths 5.4 million
  - Orphaned children; 2.5 million

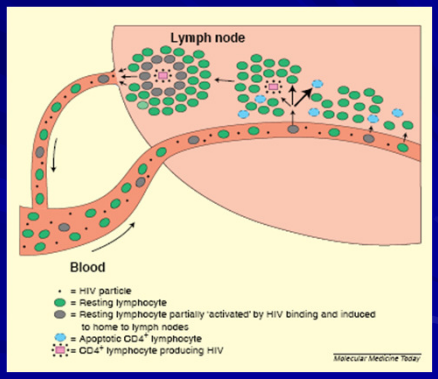
Three Different Possible Outcomes of HIV infection to a cell

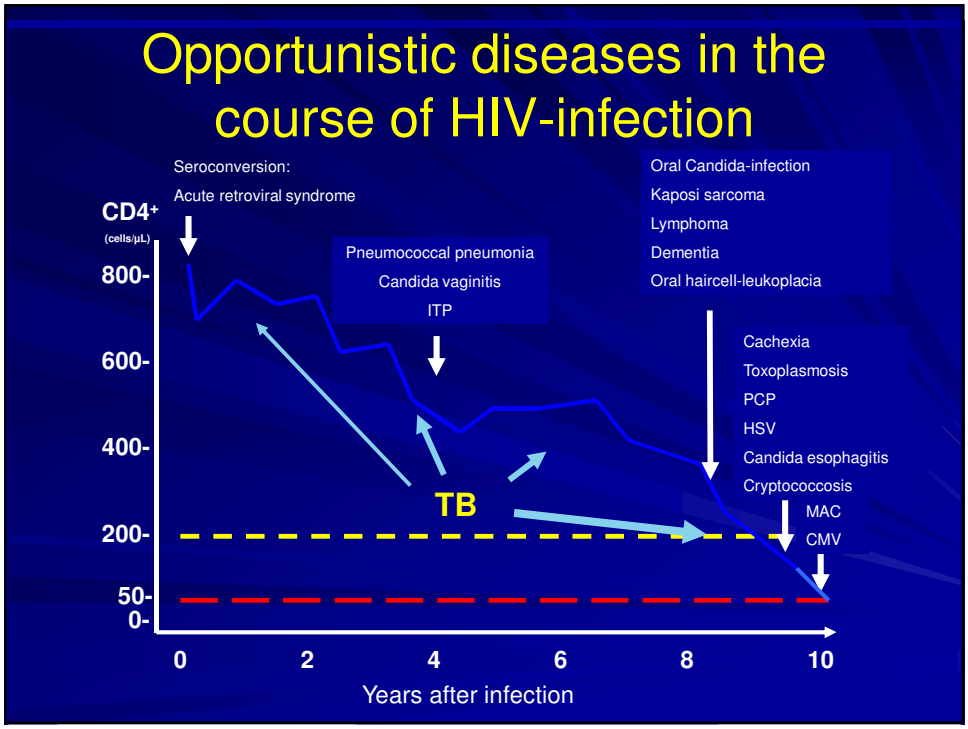
- Productive Infection
  - Occurs when activated T cell is infected, resulting in production of progeny virions
- Latent Infection
  - After viral production shuts down at end of production phase
- Abortive Infection
  - When resting T cells (comprise > 98%) is infected

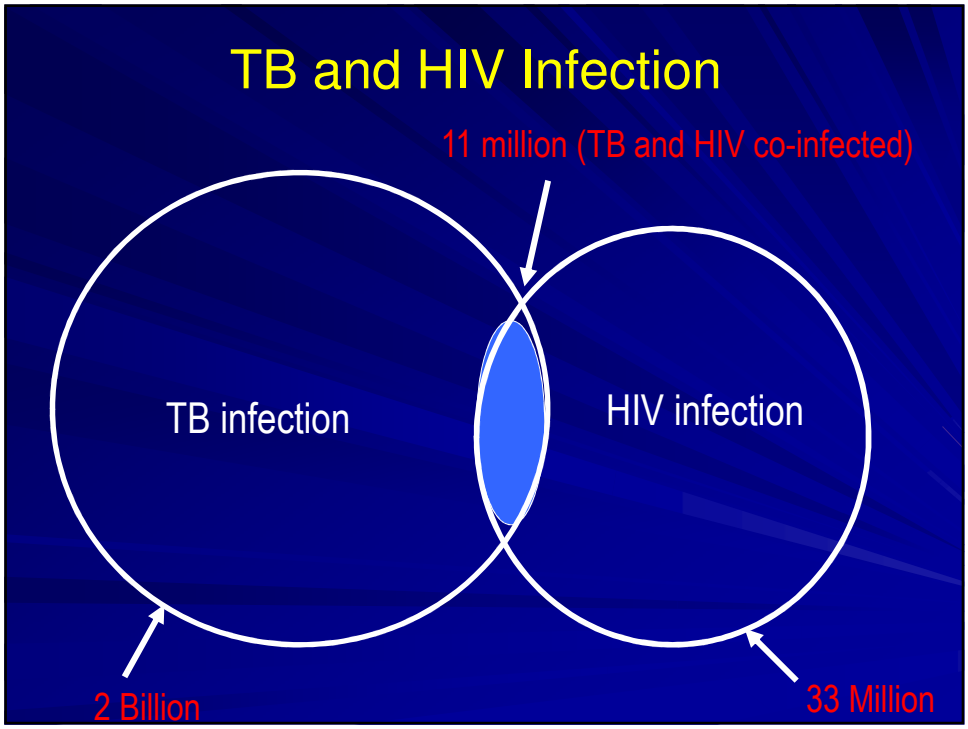
Three possible ways by which CD4 T cells could disappear from the blood:

- **The immune system stops making new CD4 cells**
- **CD4 cells die in the blood**
- **CD4 cells leave the blood**






Opportunistic diseases in the course of HIV-infection
Seroconversion:
Acute retroviral syndrome
CD4+
(cells/µL)
800-
600-
400-
200-
50-
0-
Pneumococcal pneumonia
Candida vaginitis
ITP
TB
Oral Candida-infection
Kaposi sarcoma
Lymphoma
Dementia
Oral haircell-leukoplacia
Cachexia
Toxoplasmosis
PCP
HSV
Candida esophagitis
Cryptococcosis
MAC
CMV
0
2
4
6
8
10
Years after infection

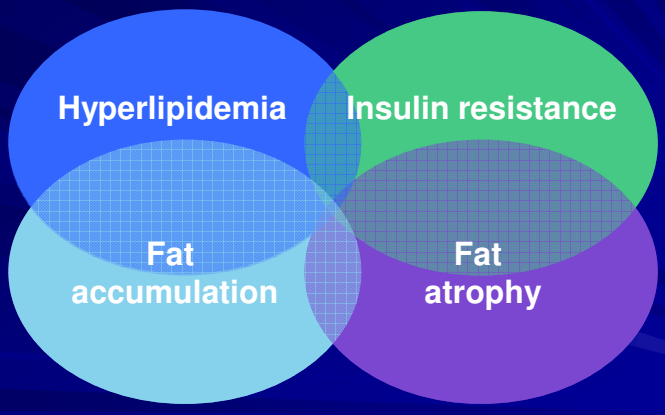

TB and HIV Infection
11 million (TB and HIV co-infected)
TB infection
HIV infection
2 Billion
33 Million

Adverse Drug Effects

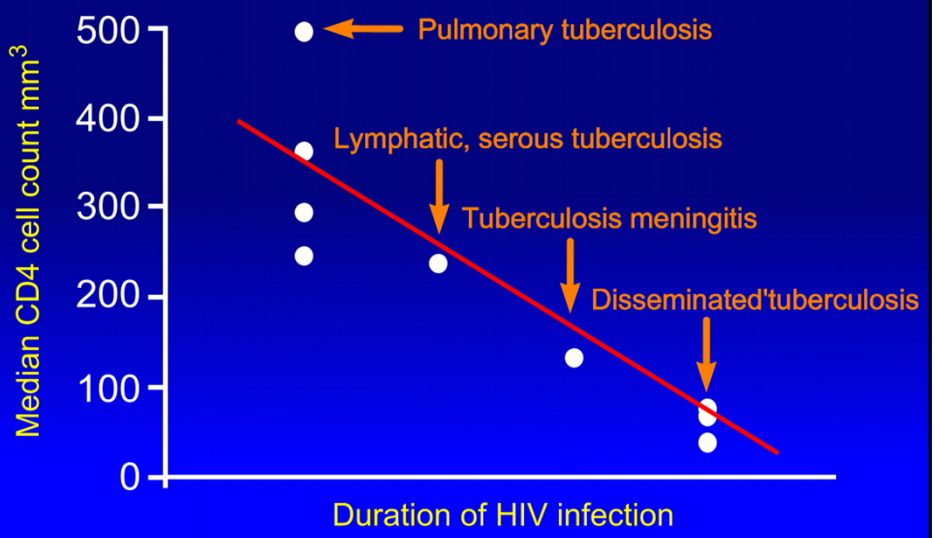
Mitochondrial dysfunction	*Metabolic abnormalities*	*Hematologic complications*	*Allergic reactions*
Lactic acidosis Hepatic toxicity Pancreatitis Peripheral neuropathy	Lipodystrophy ▪Fat accumulation ▪Lipoatrophy Hyperlipidemia/ ? Premature CAD Hyperglycemia Insulin resistance/DM Bone disorders: oesteoporosis and osteopenia	Bone marrow suppression	Hypersensitivity reactions Skin rashes

HAART INCREASES INCIDENCE OF NADC!!

HIV-Associated Lipodystrophy



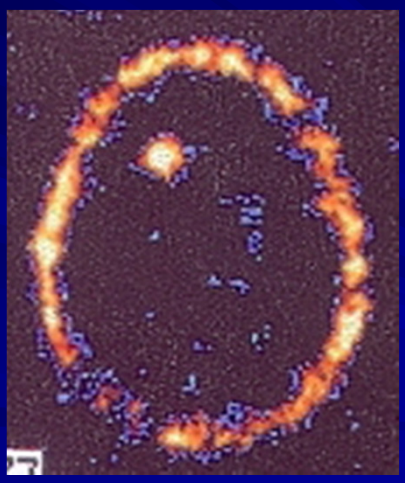
Clinical and immunopathological course of HIV associated TB



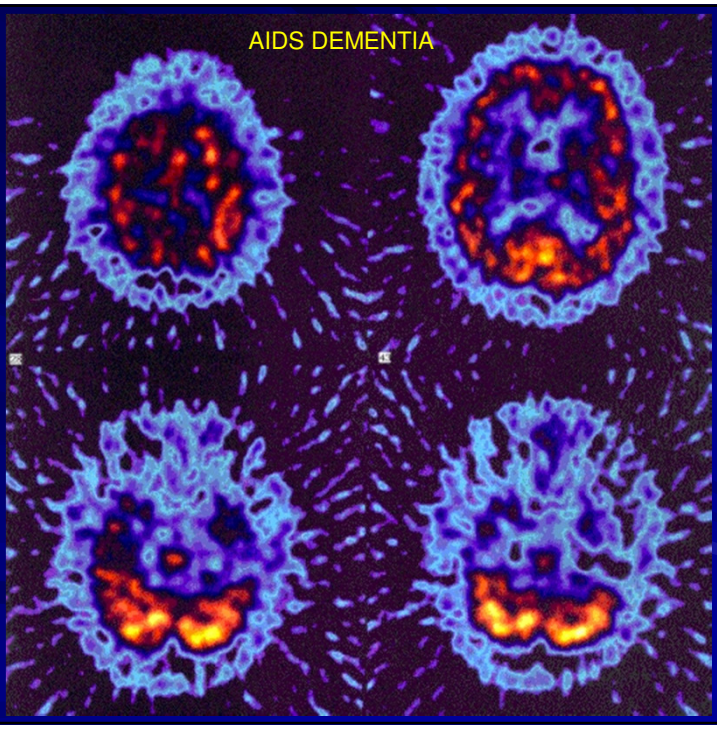
Neurological Manifestations

Acute Phase	Latent Phase	Late Stage
Myelopathy Peripheral neuropathy Brachial neuritis Cauda equina syndrome Guillain-Barré syndrome Encephalitis uncommon	Demyelinating neuropathies that resemble subacute GBS or chronic inflammatory demyelinating polyneuropathy (presenting with numbness, tingling, painful dysaesthesias & paraesthesia)	Opportunistic infections: meningitis (cryptococcal or TB), toxoplasmosis, CMV, HSV, other TB lesions Progressive multifocal leukoencephalopathy, Brain lymphoma AIDS encephalopathy or AIDS dementia complex with cognitive, motor and behavioural changes

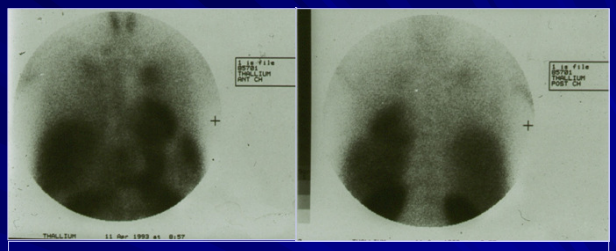
TUBERCULOMA

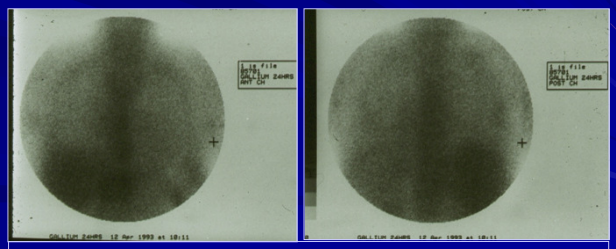


Clinical request for Toxoplasmosis vs Lymphoma



CXR, Tl, Ga



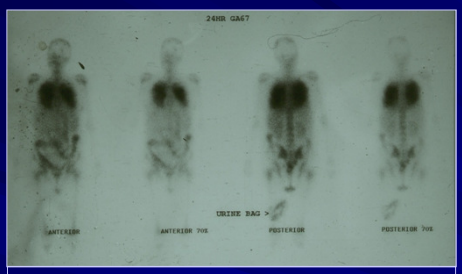


CXR – Negative
Ga67- Negative
Tl201 – Positive

Kaposi Sarcoma

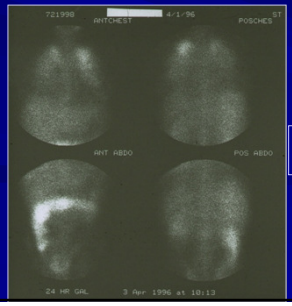
Abdel-Dayem 2004

GALLIUM IN AIDS - PCP



Severe PCP

Mild PCP



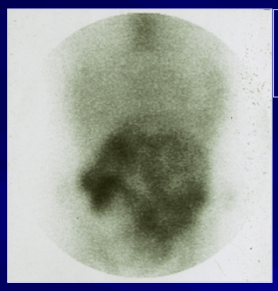
Post Treatment

Abdel-Dayem 2004

SEQUENTIAL THALLIUM AND GALLIUM SCANS IN AIDS PATIENTS

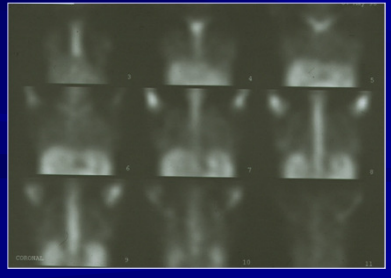
	Ga	Thallium
Kaposi	Negative	Positive
Lymphoma	Positive	Positive
Opportunistic Infections	Positive	Negative

Cryptosporoidosis



Ga – 4 hrs

Ga – 24 hrs

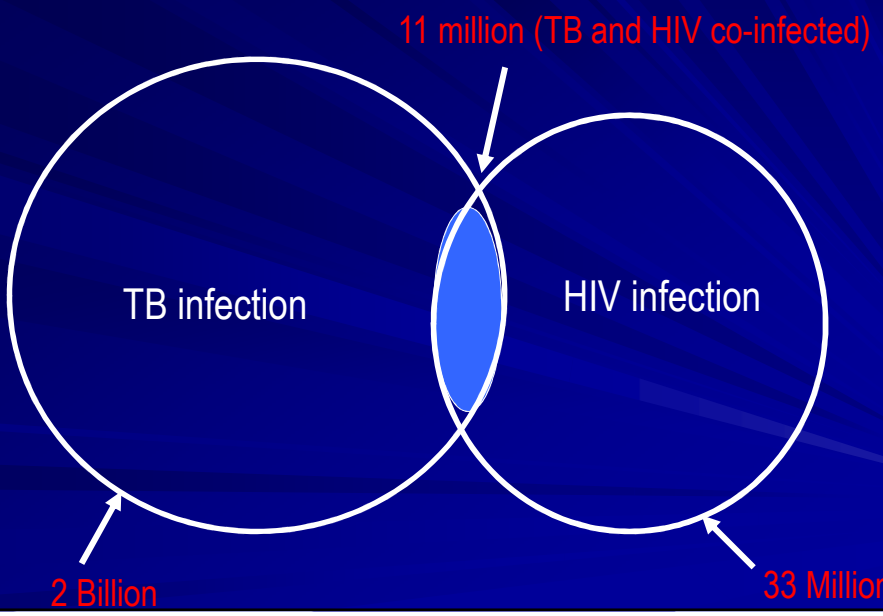


CMV

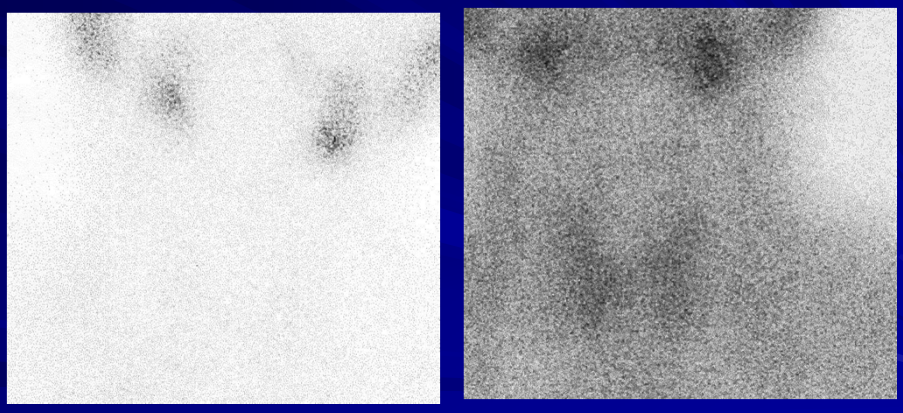
Host	Presentation
Immunocompetent	Heterophile negative mononucleosis syndrome
Immunocompromised	Retinitis Hepatitis Pneumonitis Gastritis Esophagitis Polyradiculopathy Myelitis

HIV: Opportunistic Disease CMV

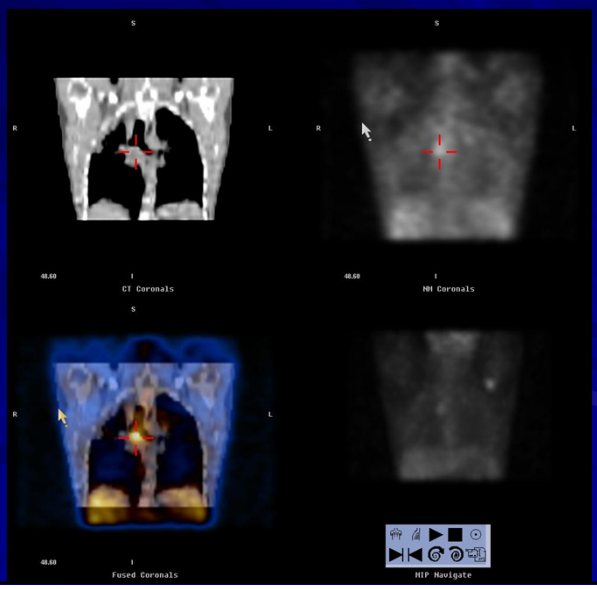
TB and HIV Infection



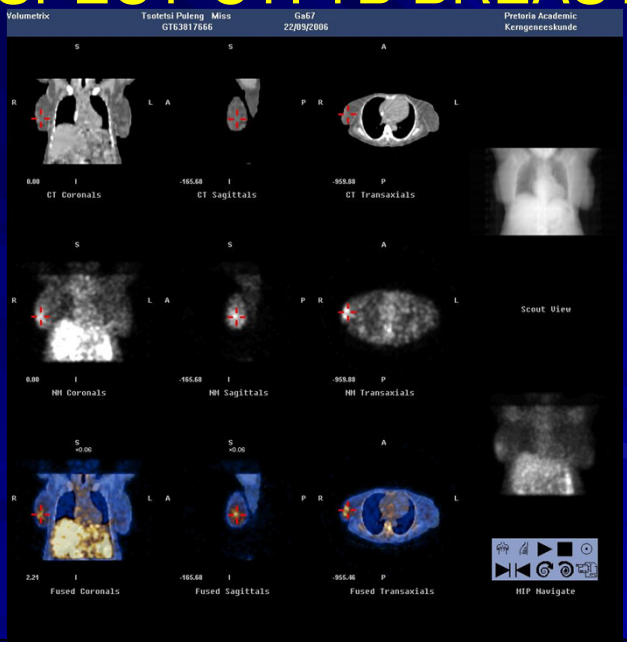
TB: THYROID



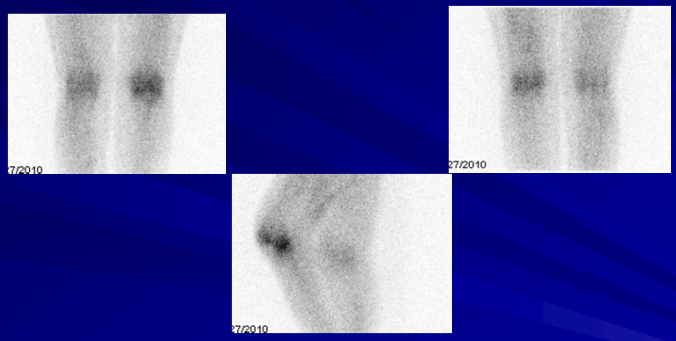
SPECT-CT: PULMONARY TB



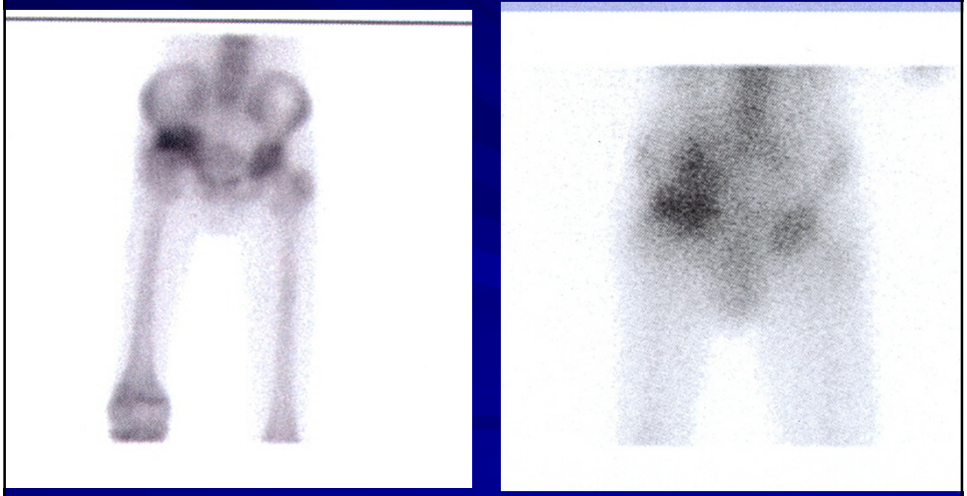
SPECT-CT: TB BREAST



Ga-67 IN HIV & Extrapulmonary TB



TB: HIP JOINT



Review HIV & FDG PET

FDG in the CNS may identify

ADC

Lymphoma vs Toxo

Nodal uptake patterns

Head & Neck: acute disease

Generalized: mid stage disease

Abdominal: late stage disease

FDG may be useful for

Staging disease

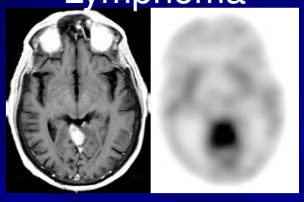
Monitoring response to therapy

FDG-PET & AIDS

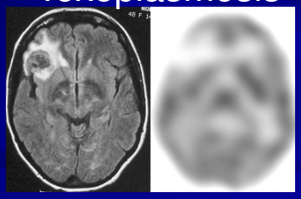
- O'Doherty et al. (J NM 1997; 38:1575)
  57 AIDS patients had body imaging
  92% sensitivity & 94% specificity for *localization* of focal pathology needing Rx.
  Intensity of uptake *not* useful for distinguishing benign from malignant processes

FDG-PET & AIDS

Lymphoma



Toxoplasmosis



Pierce et al. (Ann Int Med 1995; 123:594-598)
Hoffman et al. (J Nucl Med 1993; 34:567-575)

FDG uptake: Lipodystrophy

RESULTS

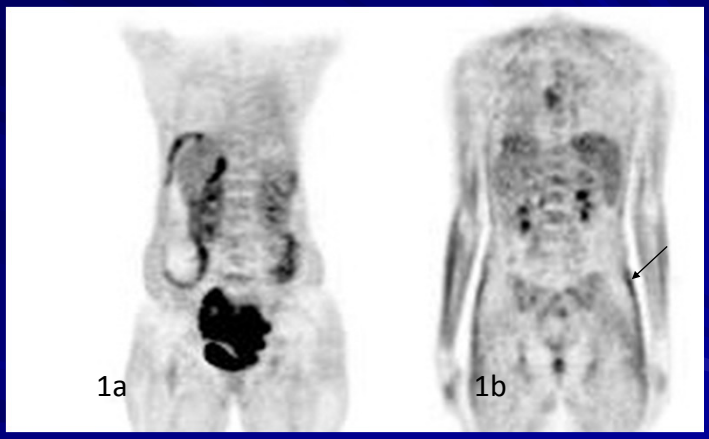
FDG uptake: Lipodystrophy vs Non-lipodystrophy

39 patients

	Duration of Rx Me/ra	SUV sc (sd)	SUV mus (sd)
Therapy Naive	-	0.34(0.14)	0.59(0.15)
No Lipodystrophy	5M(0.5-24 m)	0.46(0.24)	0.62(0.17)
Lipodystrophy	12M(6-24M)	0.9(0.15)	0.63(0.18)

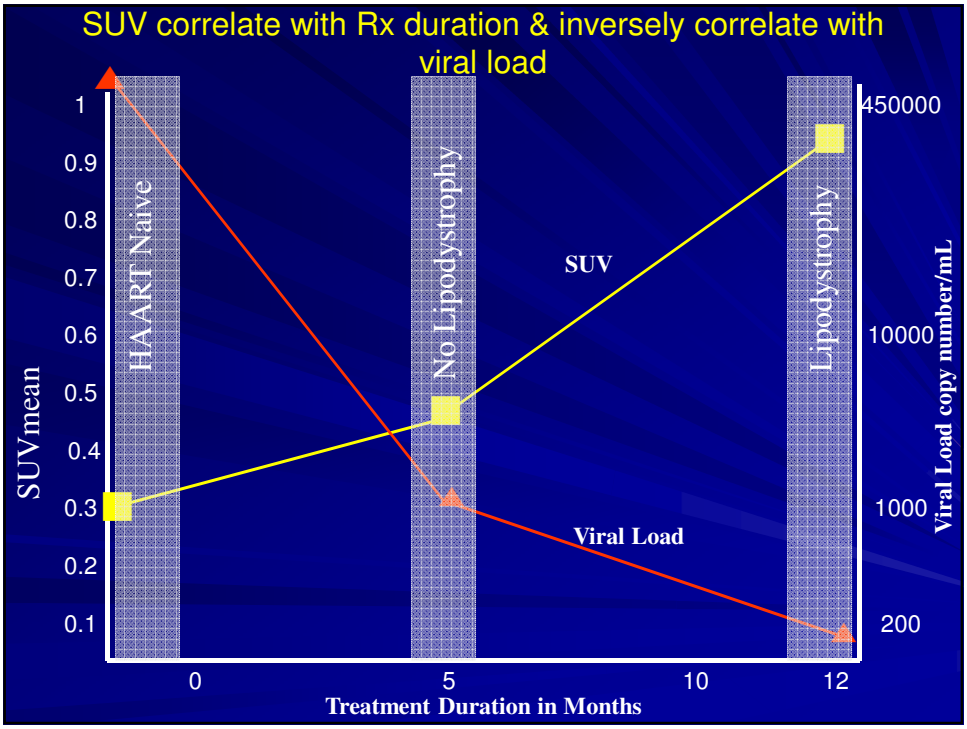
Sathekge et al., Nucl Med Commun 2010

HAART with lipodystrophy: FDG uptake in subcutaneous fat



FDG Uptake reflect ongoing apoptosis

SUV correlate with Rx duration & inversely correlate with viral load



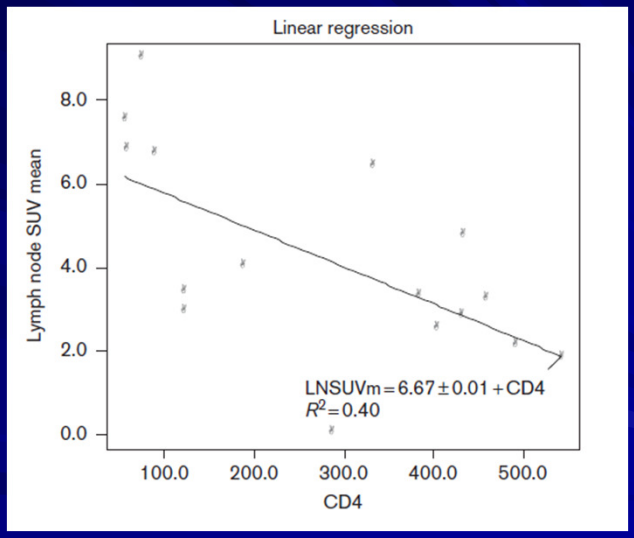
Conclusion

- FDG uptake by subcutaneous
  - ↑HIV patients under HAART presenting with lipodystrophy
  - ↓ therapy naïve HIV patients
  - ↓ patients under HAART that did not suffer from lipodystrophy.
- Contrary to available preclinical data, HAART did not influence FDG uptake by human skeletal muscle tissue under basal sedentary conditions

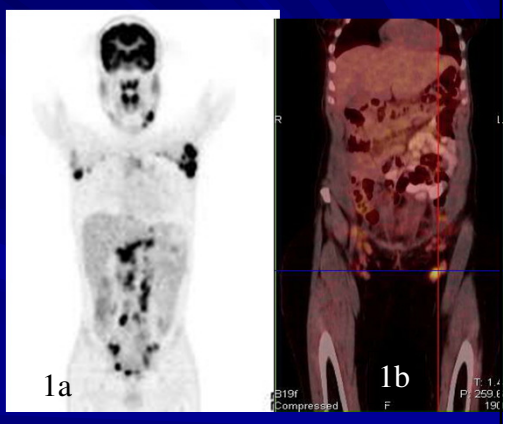
FDG Relation to CD4 & L/N Results

- Predominant sites of lymph node:
  - cervical and axillary region, followed by the inguinal
- Averaged SUVmean values:
  - 3.4 (range: 1.8-9.0).
- Median CD4 cell count :
  - 187/mL (range: 56-542 mL).
- Median viral load
  - 835 copies/mL (range: <50(0) – 457000 mL).

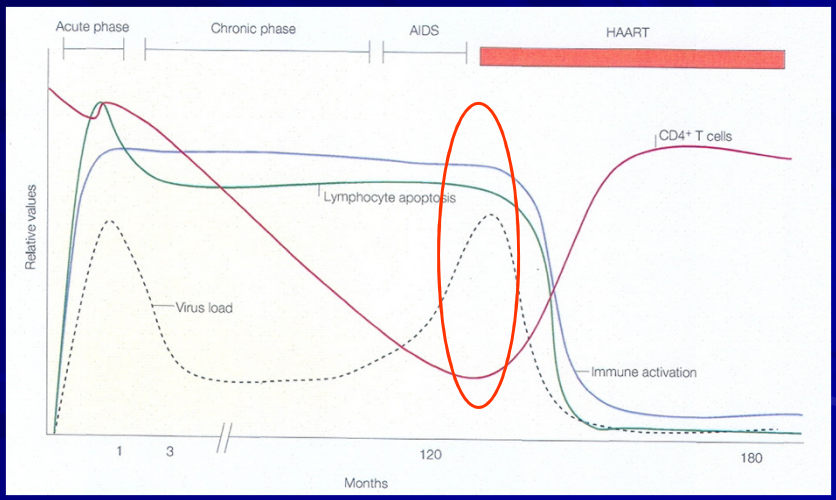
Results



Sathekge et al., Nucl Med Commun 2010



Potential Apoptotic Hypothesis



Results

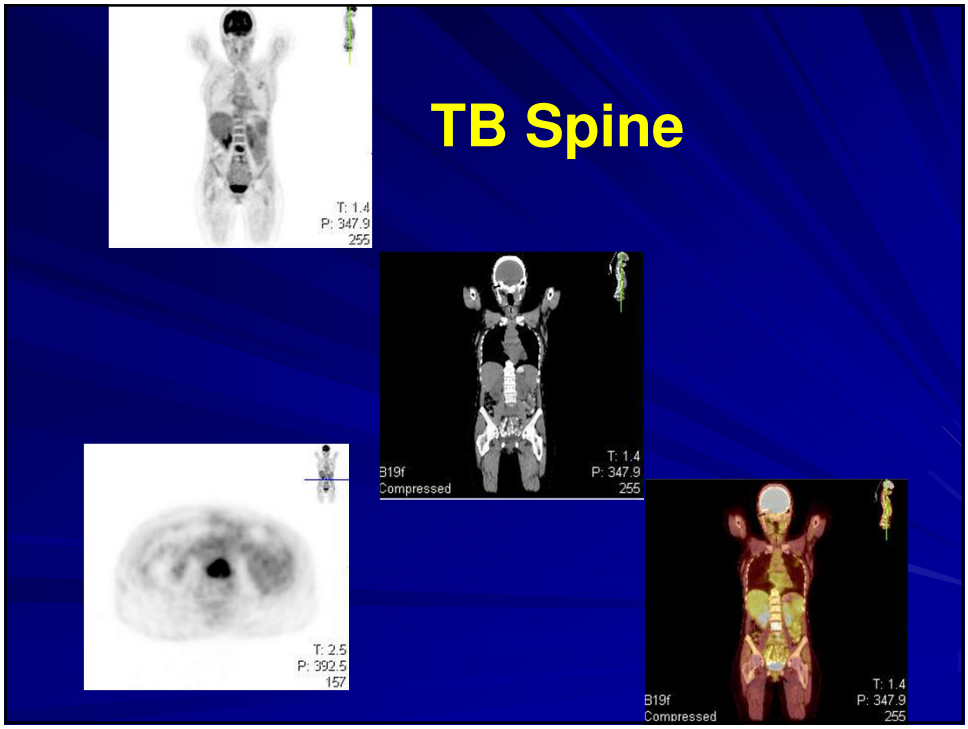
	LN (n=18)	Lung (n=5)	Pleural (n=6)	Bone (n=4)	Joints (n=3)
Early	6.3(1.6)	8.2(5.8)	1.3(0.4)	7.2 (1.3)	4.7(0.5)
Delayed	7.9(2.4)	11.1(7.2)	1.7(0.6)	10.7 (3.6)	5.2(1.4)
Ret Index	25(17.8)	35(9.0)	21(24)	45(25.5)	23(22)

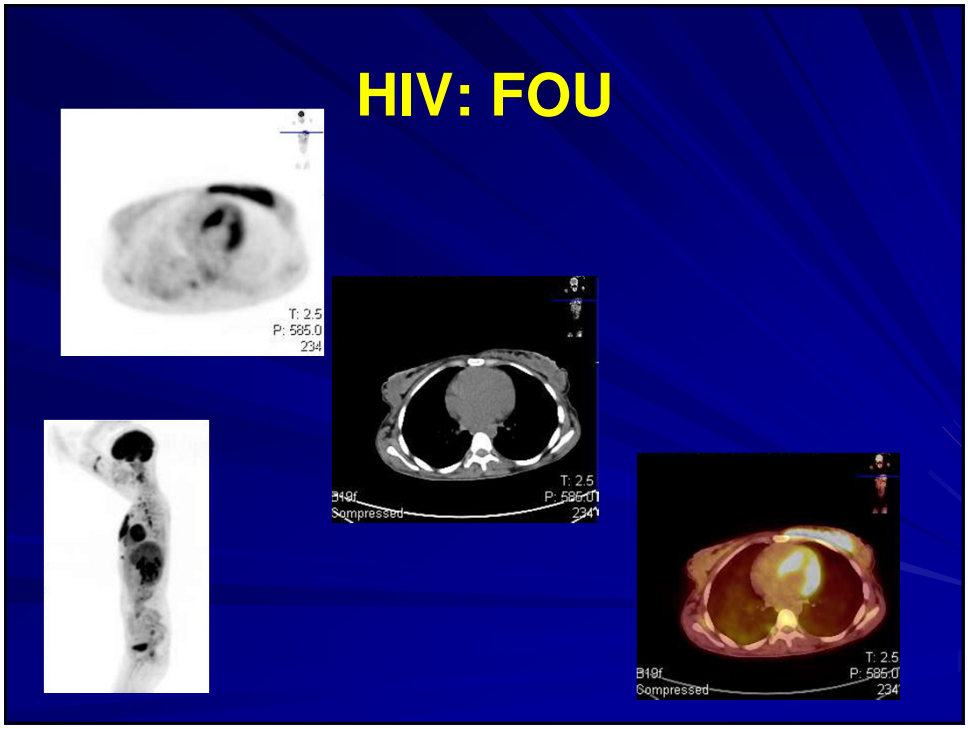
HIV & TB: Extrapulmonary TB
Results

- PET vs CT
  - PET demonstrated 50% more lymph nodes than CT
  - PET & CT were equal for lung(Diff.Act. 2/5 pts)/osseous/joints
  - PET was inferior to CT for pleural involvement
- PET did not alter the therapy planning

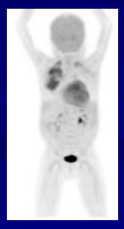
Sathekge et al., Nuklearmedizin 2010

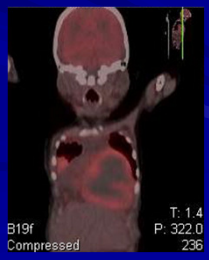
TB lymphadenitis


TB Spine
T: 1.4
P: 347.9
255
B19f
Compressed
T: 1.4
P: 347.9
255
T: 2.5
P: 392.5
157
B19f
Compressed
T: 1.4
P: 347.9
255


HIV: FOU
T: 2.5
P: 585.0
234
T: 2.5
B19f
Compressed
T: 2.5
B19f
Compressed

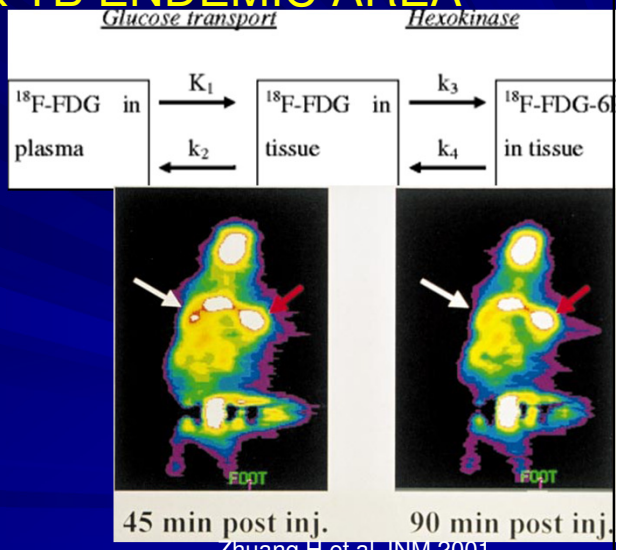
HIV: TB Pericarditis





FDG PET FOR ONCOLOGY IN HIV & TB ENDEMIC AREA

- **Drawback**
  in oncology
  diagnosis/staging



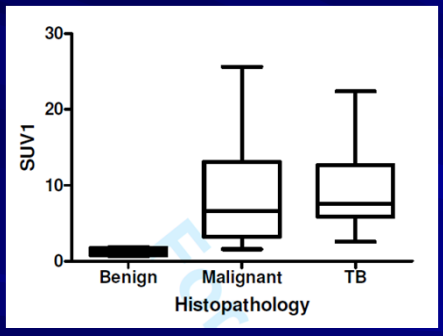
Zhuang H et al JNM 2001

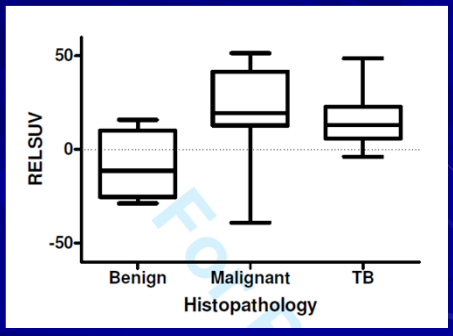
Dual-Phase FDG PET

Dual-phase imaging & SUV max not helpful in TB

SUV1max > 2.5:
sens =85.7 %, spec =25%.

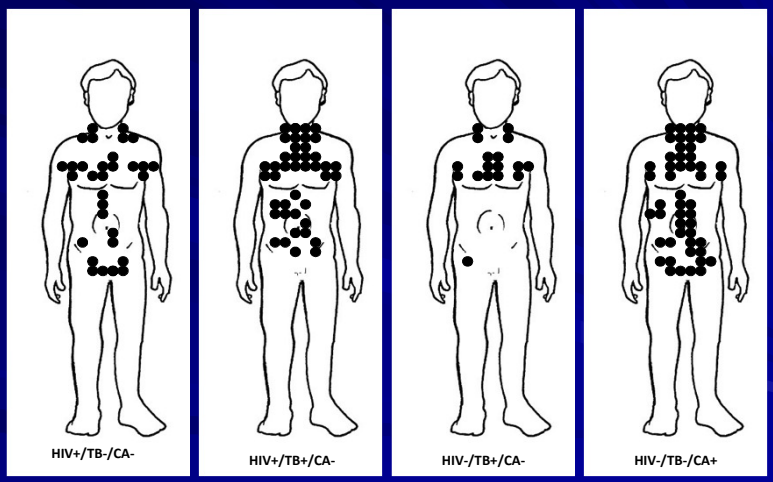
Ret index>10%:
sens =85.7 %, spec =50%.





Sathekge et al: SAMJ

Staging (L/N) in HIV & TB
Results



Sathekge et al., Q J Nucl Med

Results

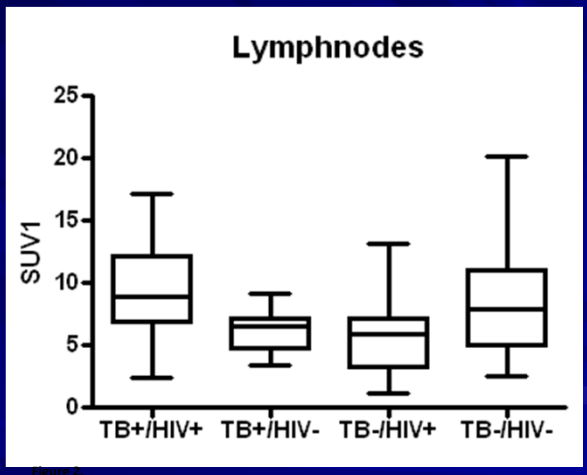
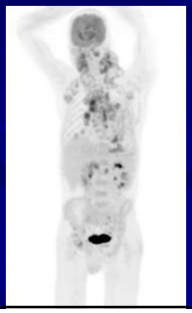
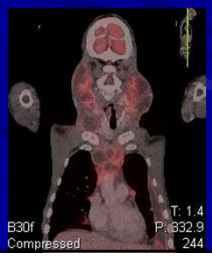


Figure 2:

Sathekge et al., Q J Nucl Med

HIV & TB L/N

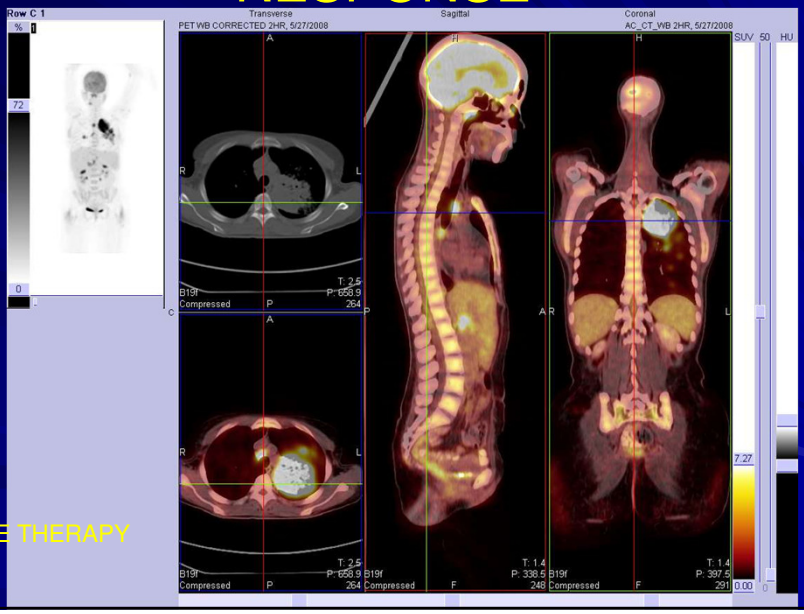




Conclusion

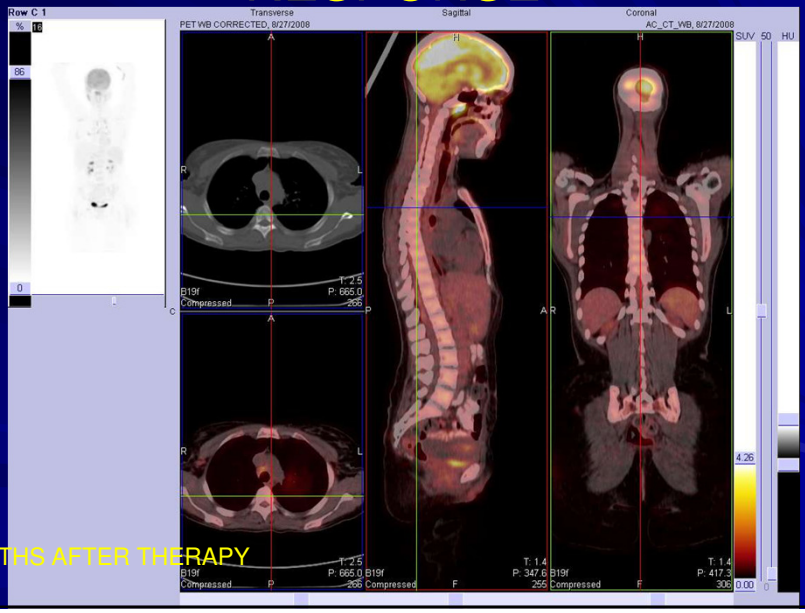
- Patients presenting with both HIV and TB (HIV+/TB+/CA-) present with significantly more sites of LN involvement and LNs involved are also metabolically more active when compared to HIV+/TB-/CA- and HIV-/TB+/CA patients.
- A significant difference in FDG uptake by LNs could be only documented between HIV+/TB-/CA- patients and HIV-/TB-/CA+ patients.
- FDG PET is not reliable for assessing malignant lymph node involvement in HIV+, TB+ or HIV+/TB+ patients with VL is not 0.

TB: MONITORING THERAPY RESPONSE



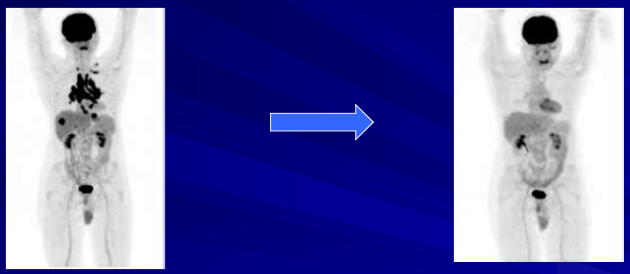
BEFORE THERAPY

TB: MONITORING THERAPY RESPONSE



3 MONTHS AFTER THERAPY

HIV: NHL – Follow-up



Immuno-virological status

What about IRIS

- SAPIT in South Africa *with interim data on mortality rates indicating a 55% reduction of mortality in the integrated TB-HIV arm*

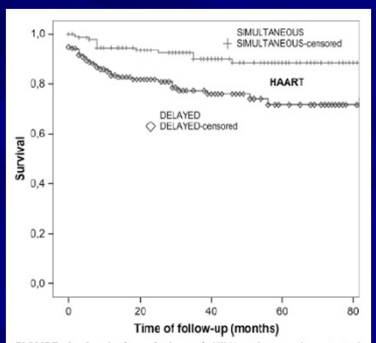


FIGURE 1. Survival evolution of HIV patients who started HAART and TB treatment at the same time (simultaneous) or after ≥3 months (delayed). Follow-up after the diagnosis of TB. Log-rank (Mantel–Cox) $P = 0.003$.

Velasco M et al., *J Acquir Immune Defic Syndr* 2009

Integrated TB-HIV arm: IRIS or Failure to Respond?

Importance of FDG PET in HIV & TB

- **Improve treatment strategy in both HIV & TB** *New Probes Indicated*
- **Improve TB diagnosis in HIV-infected patients, extrapulmonary TB**
- **Pathophysiology of IRIS to improve its DX/prognosis & Rx**

(without information ⇨ incoherent conclusion)