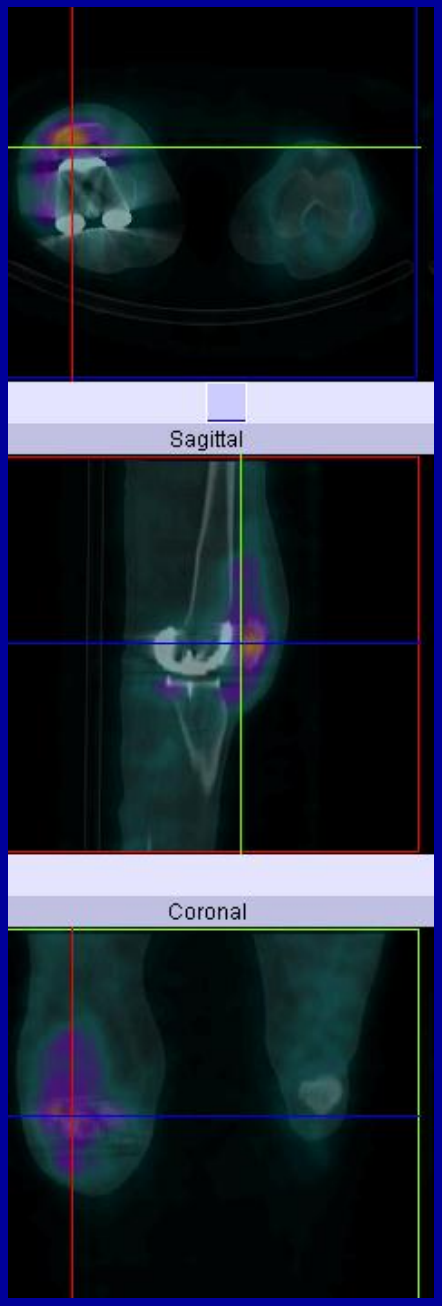
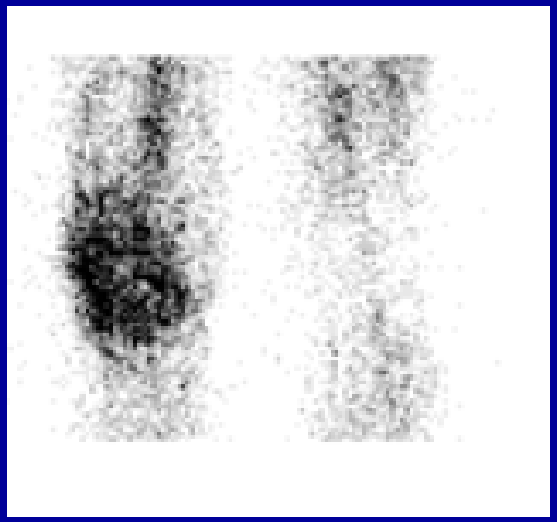



# Inflammation and infection imaging



Assoc. prof. V. Marković, MD, PhD

Assoc. prof. A. Punda, MD, PhD

A. Barić, MD, nucl. med. spec.

# Inflammation and Infection

**Inflammation** is a tissue response to the products of injury (trauma, foreign particles, ischemia and neoplasm) that attracts cells of the immune system, specialised serum proteins and chemical mediators to the site of damage.

**Infection** implies the presence of microorganisms.

**Infection** is usually associated with inflamation, the reverse is not always true.

**The inflammatory** response is associated with increased blood flow, increased vascular permeability and migration of leukocytes out of blood vessels into the tissues (chemotaxis). Plasma carries proteins, antibodies, and chemical mediators that modulate the inflammatory response to the site of infection.

# Inflammation and infection scintigraphy

- **Radiolabeled leukocytes-** Tc-99m-HMPAO (hyxamethyl propyleneamine oxime) or In-111-oxine/tropolone: chemotaxis, adhesion, diapedesis
- **Tc-99m- labeled antigranulocyte antibodies**; bounding on granulocyte antigen NCA-95, capilary premeability
- **Ga-67-citrate**; transferrin and lactoferrine receptors
- **Tc-99m-nanocolloid** (bone marrow scintigraphy): capilary premeability and phagocytosis in bone marrow reticuloendothelial cells
- Tc-99m or In-111 labelled polyclonal **immunoglobuline**; capilary premeability
- **FDG-PET**
- **Tc-99m-diphosphonate scintigraphy-** inflammatory bone and joint diseases

# Scintigraphy in inflammatory disease

- Indication:

- localisation of unknown inflammatory focus

- dif. dg. of certain inflammatory foci wich can not be seen using standard diagnostic procedure

- follow-up in chronic inflammatory diseases with exacerbations

- most commonly: bones and joints, bowel, fever of unknown origin (FUO)

# Inflammation

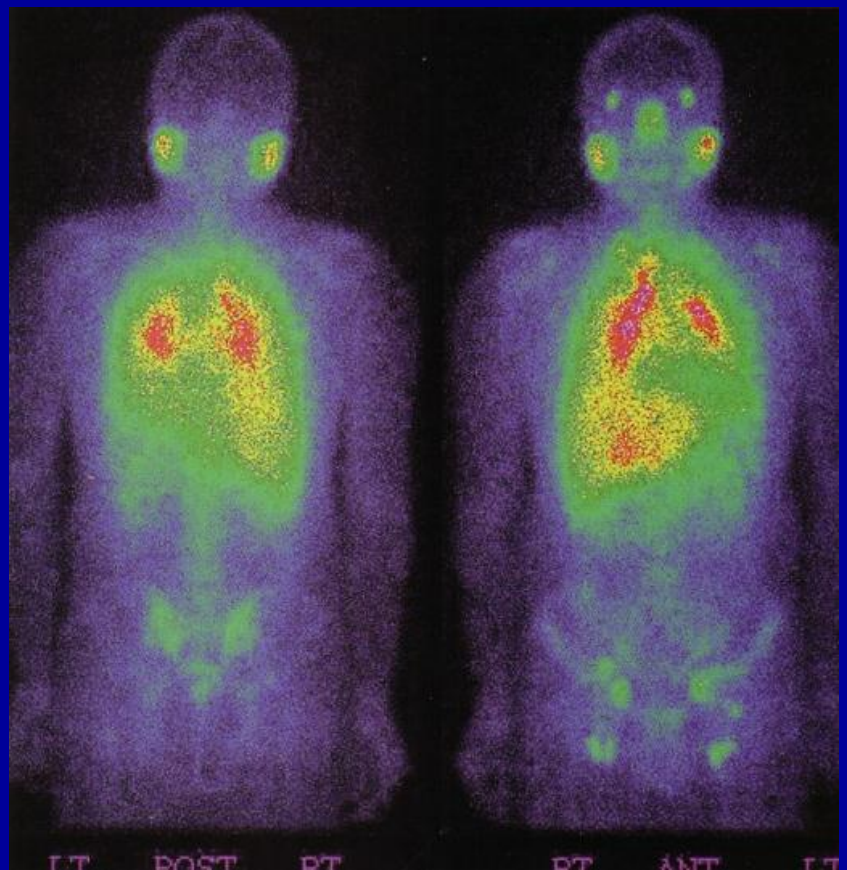
- Ga-67 is less significant diagnostic procedure after labeled leukocytes and leukocyte monoclonal antibodies have been developed

- Abscess: if it cannot be seen using standard dg methods

- Osteomyelitis, hilar sarcoidosis, immunocompromised patients and AIDS (pneumocystis carini and CMV pneumonia)

# GALLIUM -67-CITRATE SCINTIGRAPHY

## Dg. of inflammatory disease



# Gallium-67 and its biodistribution

- Gallium is chemical element in group 13 of the periodic table (In, Al), cyclotron-produced (from Zn-68)
- Y rays: 93 (38%), 184 (24%), 296 (16%) i 388 (4%) keV; $T_{1/2}$ = 78 hours
- It is used in form of citrate, intravenous
- Adults: 3-5 mCi
- Children: 0.04- 0.07 mCi/kg, minimum 0.25 mCi
- Time of the scan- tumors: 48-72 h post injection
- Time of the scan- infections: 6-24 h post injection

# Gallium 67

- Inflammation: fever of unknown origin (FUO), osteomyelitis, sarcoidosis, HIV positive ...

# Ga -67 at the site of inflammation

- Forms complexes with plasma transferrin that act as carriers for 67Ga to sites of inflammation
- It is incorporated into leukocytes, bound by intracellular lactoferrin, which then migrate to inflamed areas
- Bindes to siderophores produced by the bacteria, so it may been taken up by pathogenic microorganisms themselves

# Physiological 67-Ga distribution

- Nasopharynx, lacrimal and salivary glands
- Sternum
- Liver
- Spleen
- Kidneys, bladder (first 24 h)
- Bowel (during few hours post injection)
- Heart and great vessels (during first 4-6 h)

# Patient preparation and scintigraphy

- Medium energy parallel collimator, large field of view gama camera
- Patient preparation with laxative (night before scan)
- Photopeak on 93, 184, 296 i 388 keV
- Patient is in supinated position, mediastinum, abdomen

# INDICATIONS

- **Liver abscess**: Tc 99m Sulfur Colloid subtraction images
- **Retroperitoneal abscess, kidney infections**– persistent renal acitivity after 24 h, increasing uptake
- **The assessment of inflammatory activity in case of inflammatory lung diseases:** sarcoidosis, TBC, bacterial pneumonia, vasculitis, idiopathic pulmonary fibrosis
- **Acute inflammatory disease of the heart and pericardium**

Abnormal gallium activity is equal to or greater than activity in the liver

# Gallium scan in sarcoidosis

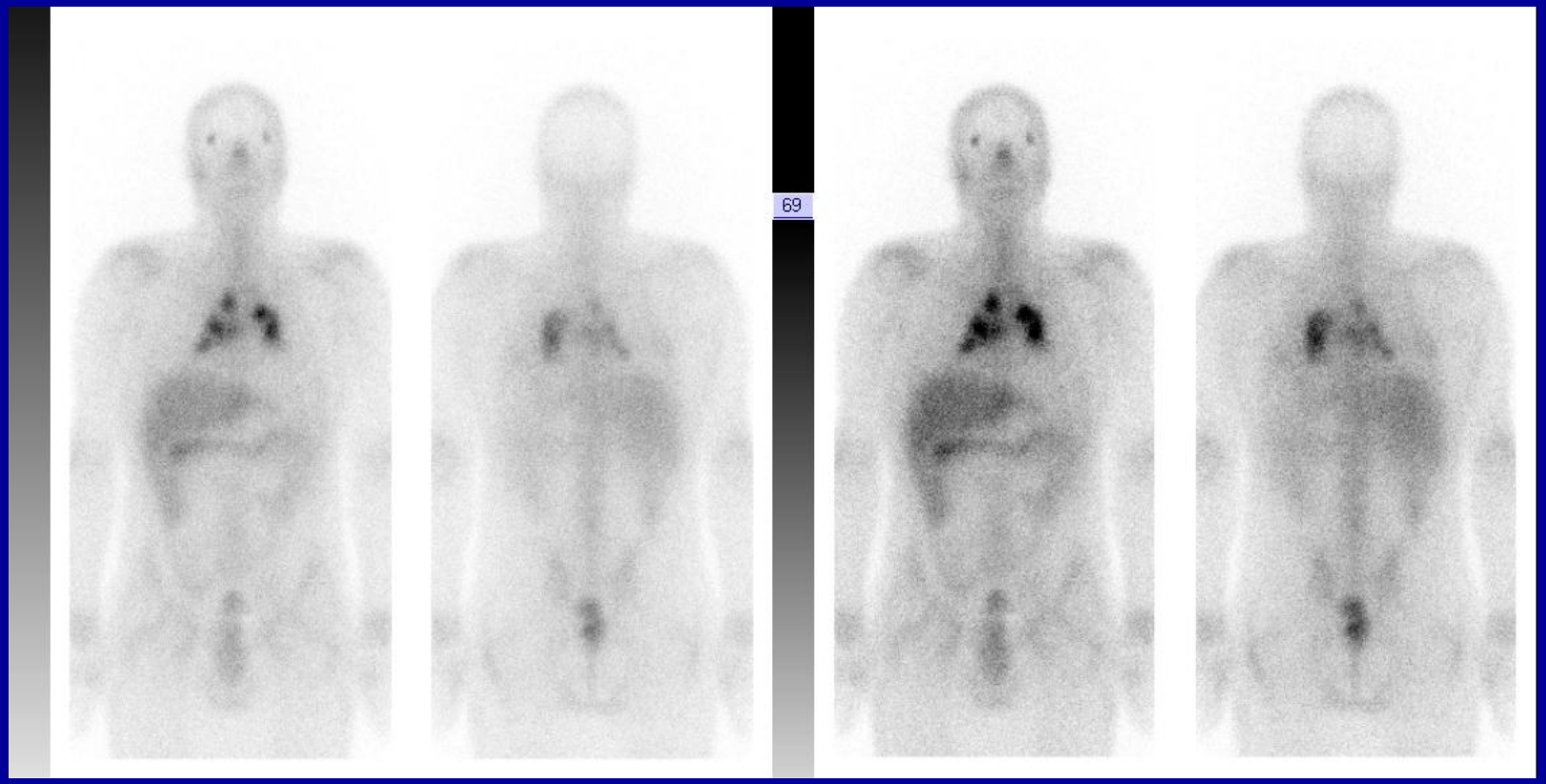
- Important to distinguish active vs inactive disease and chronic fibrosis

- Contraindications:
- Absolute: pregnancy, breastfeeding
- Relative: child age

# Sarcoidosis

- Lambda sign- increased gallium activity in intrathoracic lymph nodes bilaterally (paratracheal and hilar)
- Panda sign- symmetrically increased activity in the lacrimal, parotid, and salivary glands (may be seen in a significant percentage of patients with radiation sialoadenitis, primary Sjögren syndrome, AIDS)

# Sarcoidosis

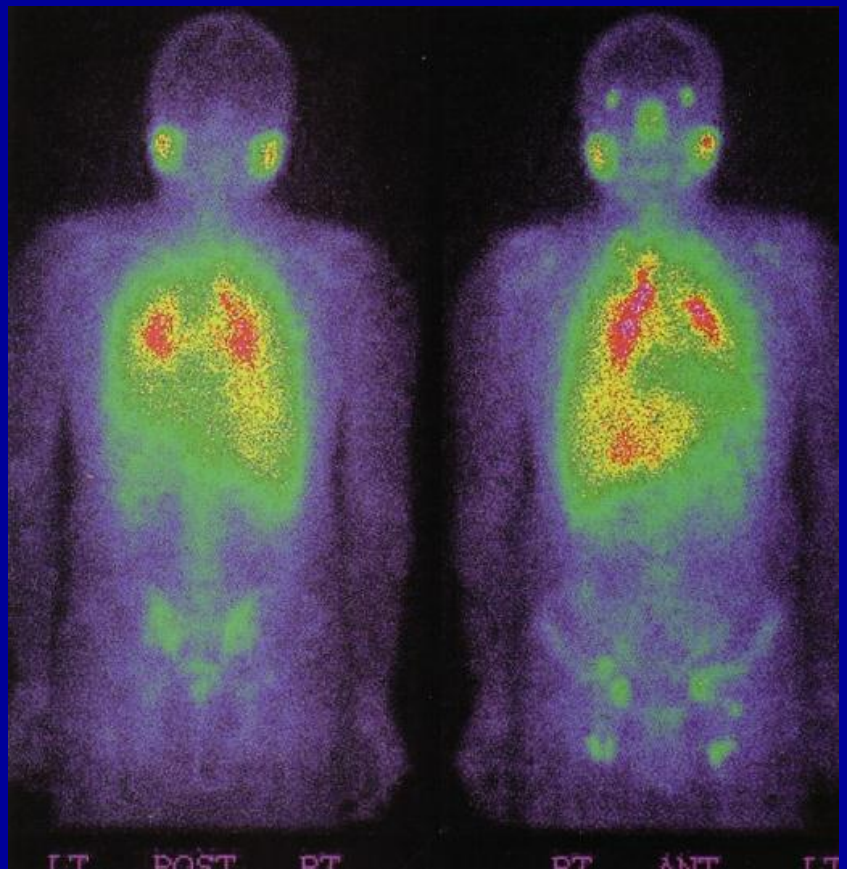



Lambda sign & Panda sign

# Sarcoidosis

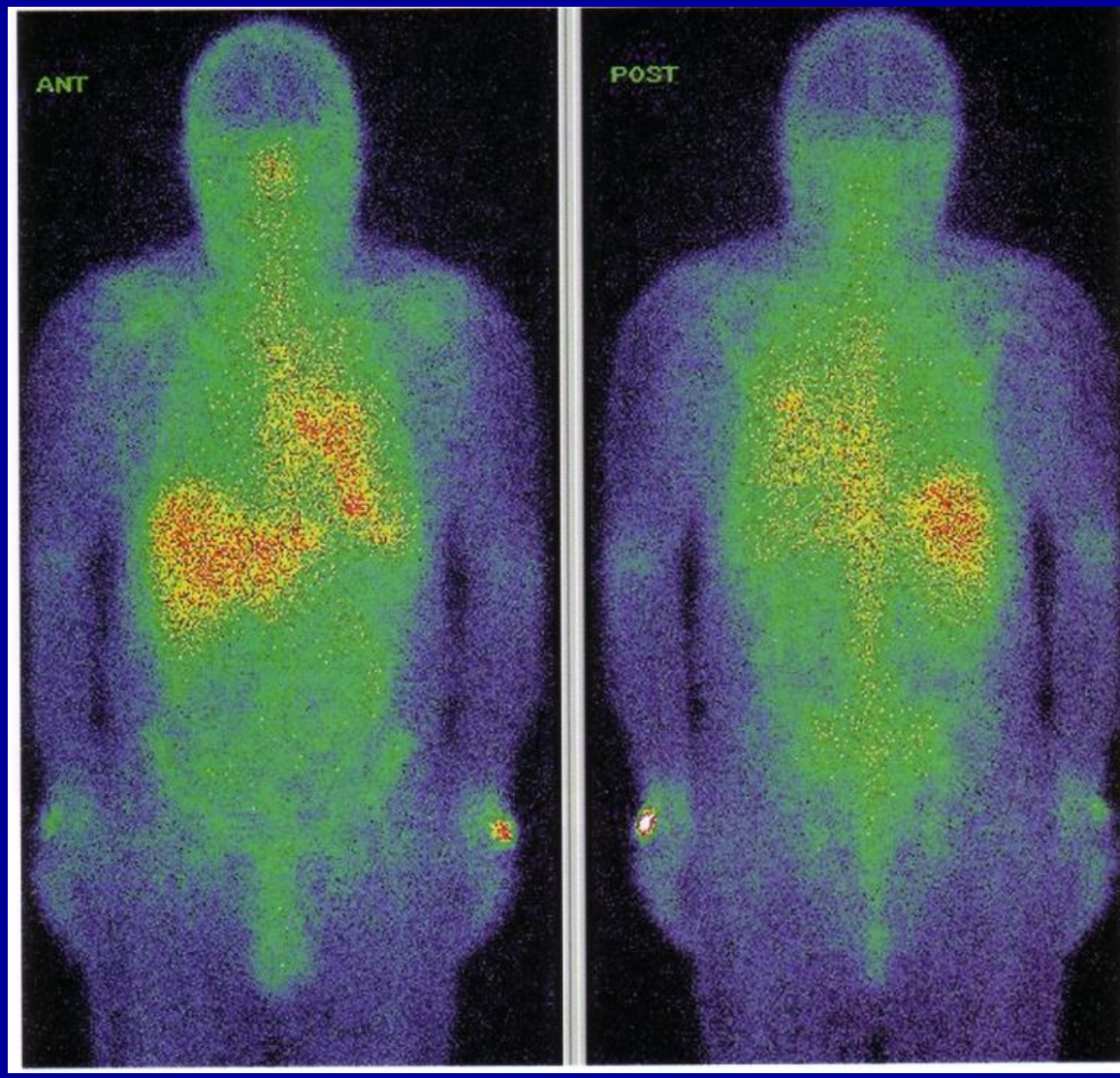
30-yr old male patient.

Increased uptake in intrathoracic ln (Lambda sign), lungs, lacrimal and salivary glands (Panda sign), right infraclavilurar region, inguinal and iliac lymph nodes (ln)



# Pulmonary TBC

Ga- 67 increased uptake in the left lower lobe of the lung



# Diagnosis of osteomyelitis

- **Nuclear medicine procedure:**

1. Bone scintigraphy /Tc-99m diphosphonate (BS)
2. Ga-67
3. Radiolabeled leukocyte scintigraphy (LS)
4. Bome marrow scintigraphy (BMS),
5. Antigranulocyte scintigraphy (AGS)
6. FDG-PET

# 1. Bone scintigraphy (BS)

- Tc-99m diphosphonate: MDP ili HDP
- osteotrophic radiotracers: accumulates on the mineral matrix surface
- widely available, relatively inexpensive, easily performed and rapidly completed
- BS is highly sensitive, but not very specific method

# 1. Tc-99m diphosphonate

- Increased uptake:

- postoperative physiological bone remodelling
- aseptic loosening
- infection
- fracture
- heterotopic ossification

# 2. $^{67}$Ga –citrate

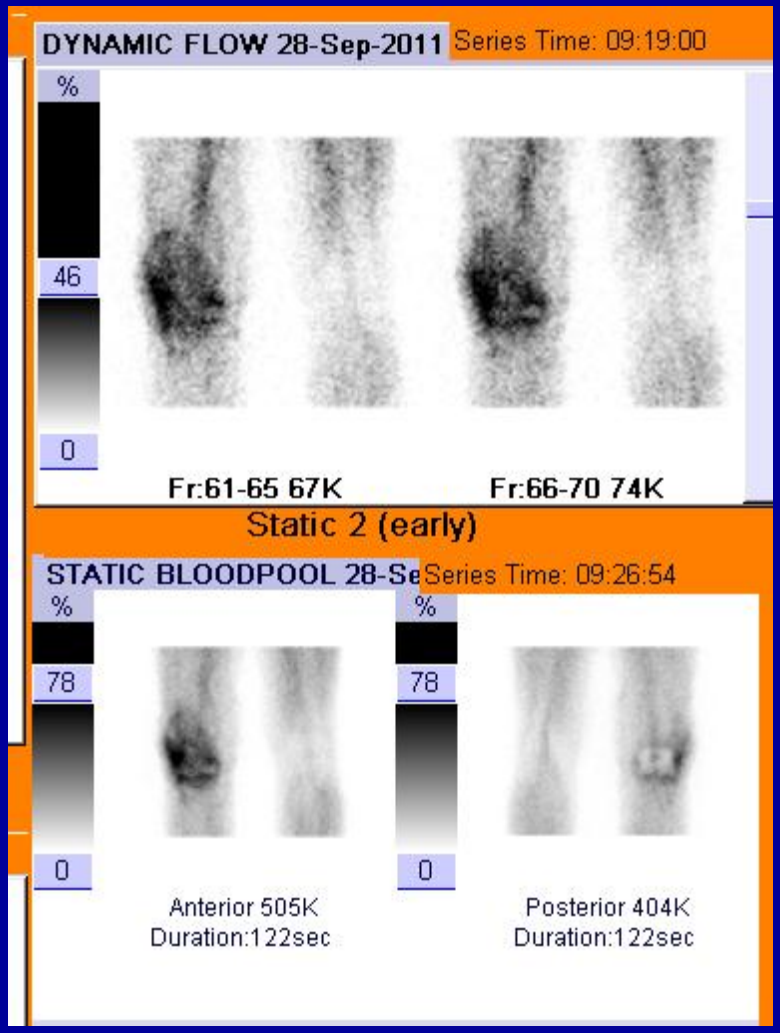
- bone-seeking radiopharmaceutical
- Usefull in combination with Tc-99m bone scintigraphy (sequential Ga/BS)
- Increased uptake:- infection
  - postoperative
  - heterotopic or periostal new bone formation
  - aseptic loosening
  - fracture
  - granulomatous reaction to prosthetic cement

# 1. and 2. Sequential $^{99m}$Tc-MDP and $^{67}$Ga citrate scintigraphy

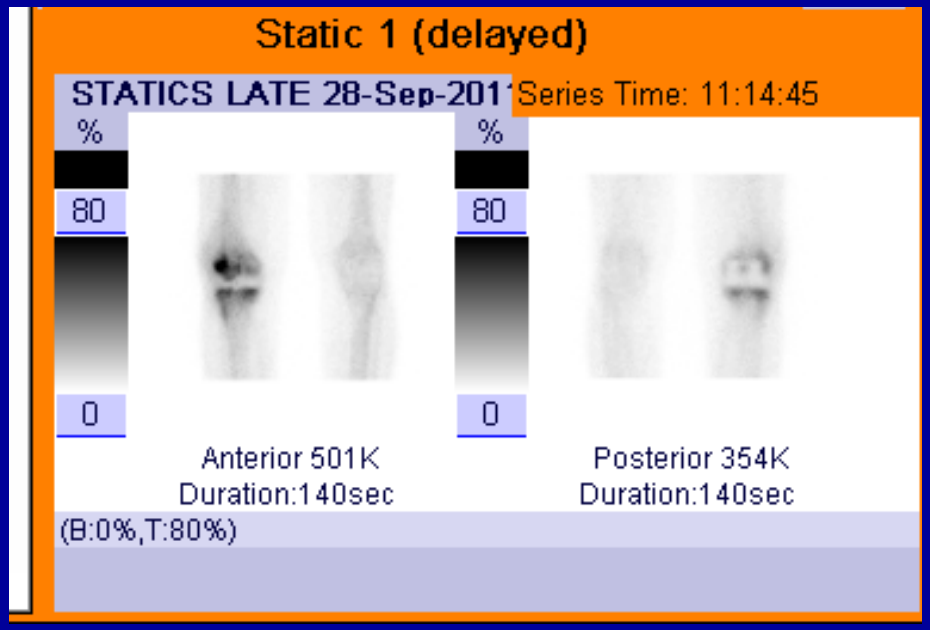
- Two separate scans
- Uptake incongruency of the spatial distribution and intensity
- Accuracy 68- 80%
- High additional radiation dose of 18 mSv

# Right knee prosthesis: osteomyelitis or aseptic loosening?

## Three-phase bone scan (99mTc-MDP)

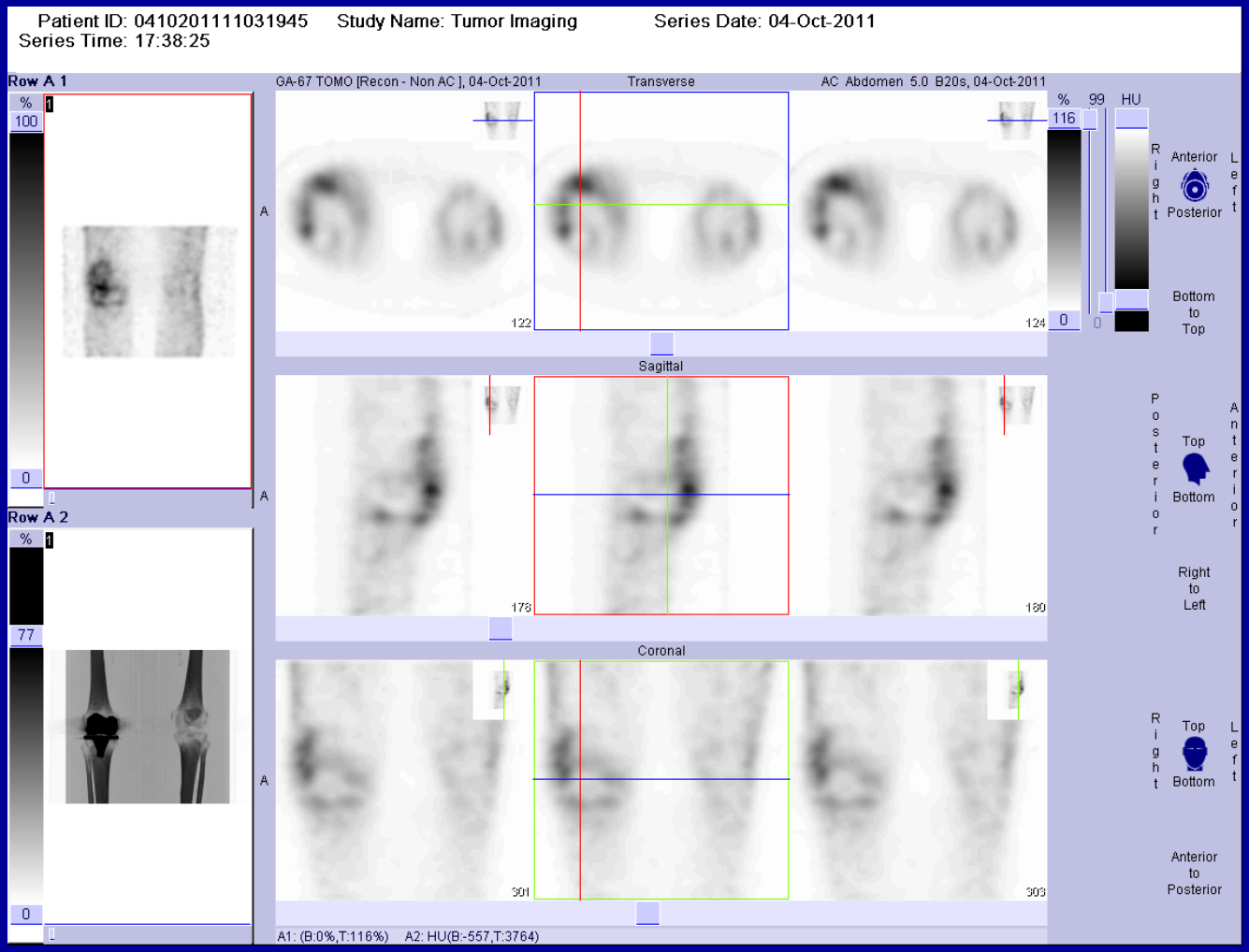



## All of three phases



# Right knee prosthesis: osteomyelitis or aseptic loosening?

## Ga-67-SPECT

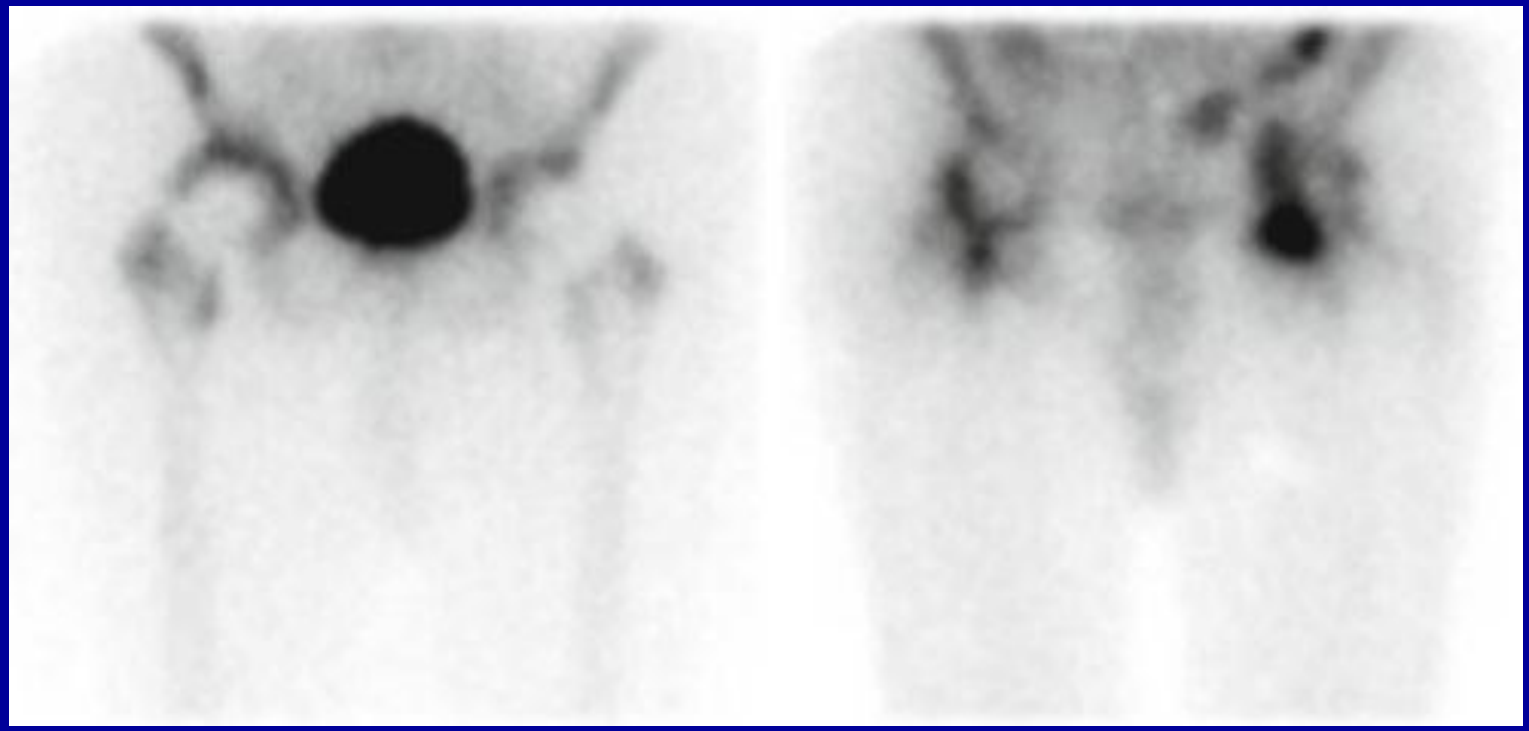


# SPECT/CT

- more exact anatomical localisation of the radiotracer uptake
- detection of tracer accumulation in bone and surrounding soft tissue
- In a case of chronic posttraumatic osteomyelitis it has clinical relevance in selecting patients for surgery
- Improves specificity compared to SPECT (78 vs 89%) while sensitivity remains equal

Tc 99-m BS

Ga 67-citrate



## Bilaterally infected 10-year-old cementless hip prostheses

The distribution of activity on the bone and gallium images is **spatially incongruent** and the combined study is **(true) positive** for infection. Intraoperative cultures grew S. aureus.

# 3. Labelled leukocyte scintigraphy

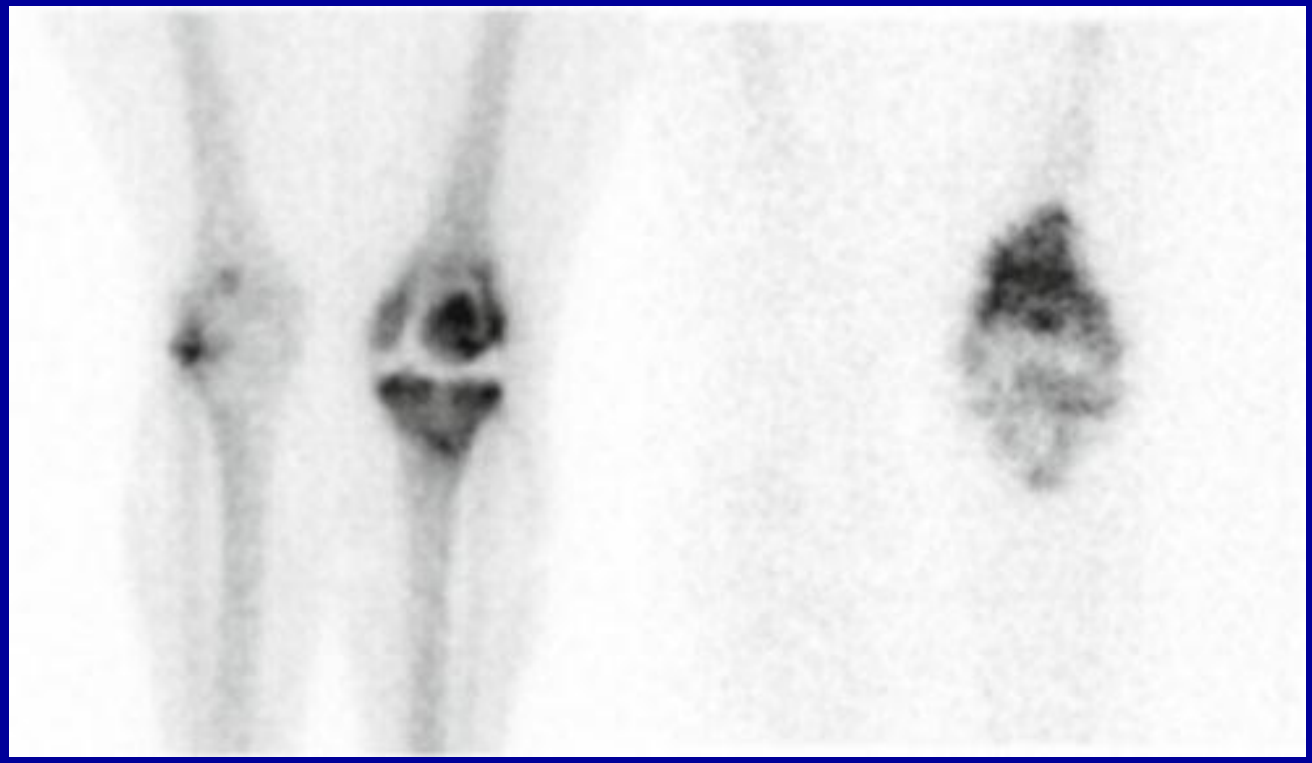
## **“the gold standard”**

- In vitro $^{111}In$ or $^{99m}Tc$ HMPAO labeling
- Labelled leukocytes do not accumulate at sites of increased bone turnover or remodeling in the absence of infection
- Unsatisfactory results due to: presence of a chronic infection and a biofilm, antibiotics, inflammation of the surrounding soft tissue

- Risk of contamination during in vitro labeling

Tc-99m-BS

Tc-99m-LS



**Infected 5-month-old left knee replacement**

The distribution of activity around the prosthesis on the bone and Tc-labelled leucocyte images is **spatially incongruent**, the usual criterion for infection.

# 3. and 4. Combinated scintigraphy: bone marrow scintigtaphy (BMS) and labeled leukocyte

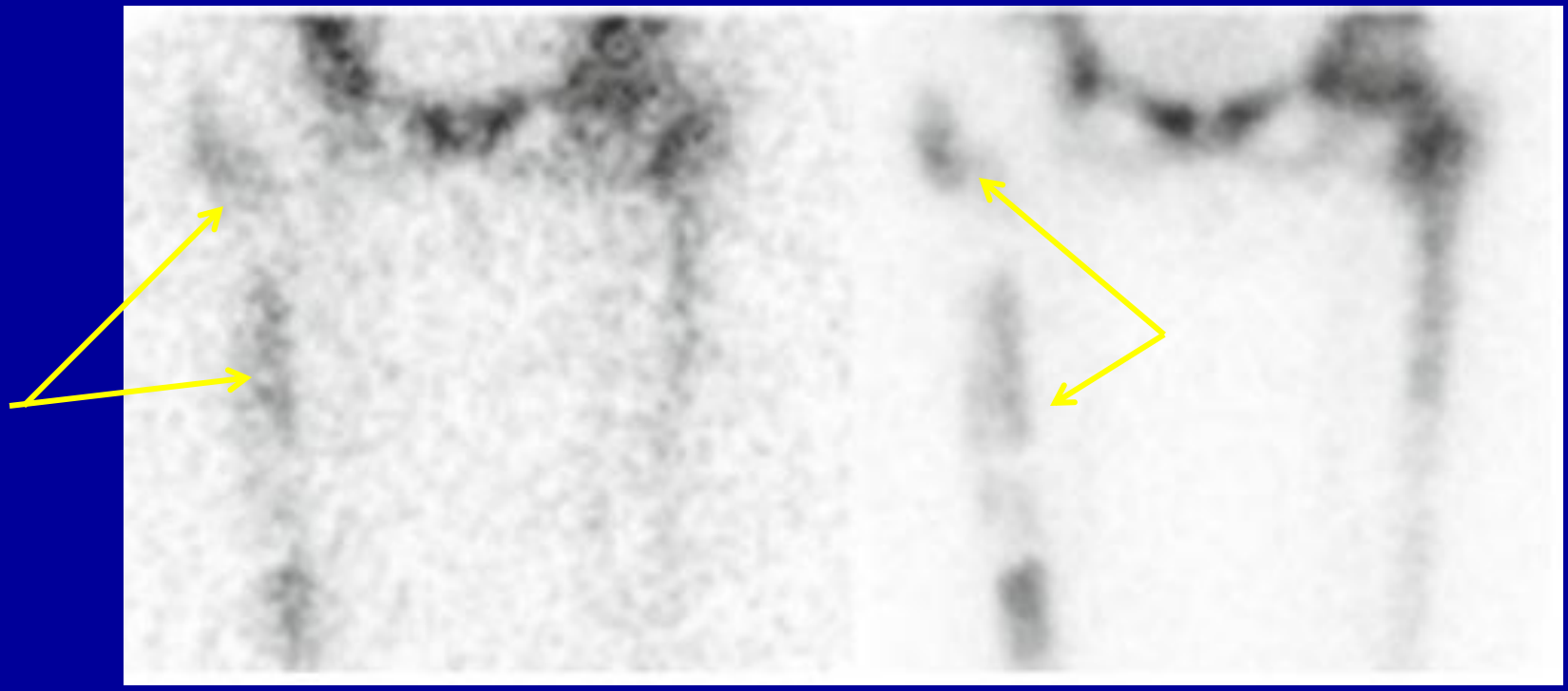
- BM (bone marrow): $^{99m}$Tc sulphur colloid (uptake in the reticuloendothelial system of the bone marrow)
- Leukocytes: $^{111}$In- HMPAO, $^{99m}$Tc- HMPAO (bone marrow, infection)
- In normal condition distribution of activity is similar
- Osteomyelitis - increased uptake of leukocytes
  - supressed uptake of sulphur colloid
  - spatially incongruent in prosthetic joint infection (PJI)

- Accuracy 86-98%

# 3. and 4.

**In-111-LS**

**BMS**
**Tc-99m-sulphur colloid**



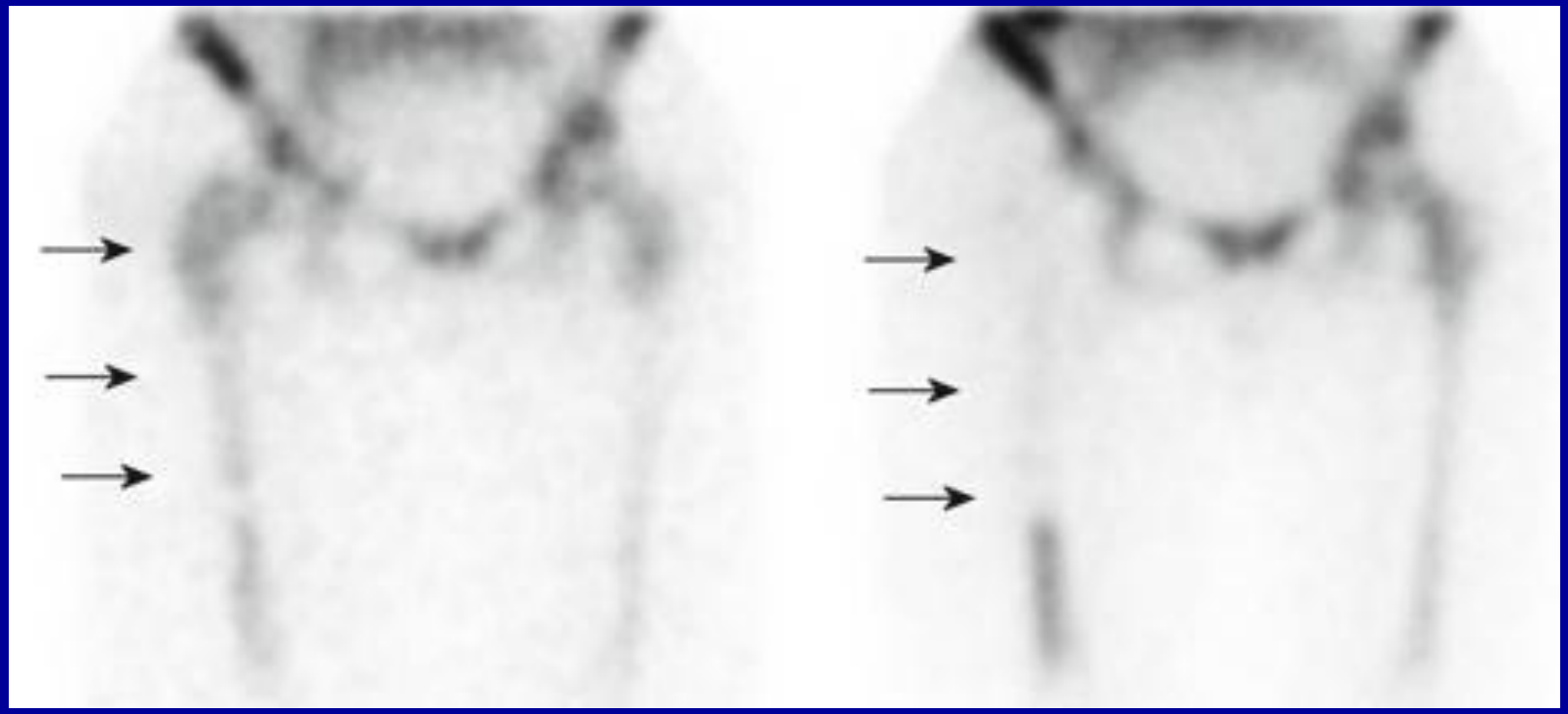
## Aseptically loosened right hip replacement

The distribution of activity around the prosthesis on the labelled leucocyte (left) and sulphur colloid (right) images is **spatially congruent**, and the combined study is **negative** for infection.

# 3. and 4.

**In-111-LS**

**BMS**
**Tc-99m-sulphur colloid**



## Infected right hip replacement

There is activity around the femoral component on the labelled leucocyte study (left). On the bone marrow image (right), however, activity is present only distal to the tip of the prosthesis. The distribution of activity on the labelled leucocyte and sulphur colloid images is **spatially incongruent** (arrows), and the combined study is **positive** for infection.

## Dual time leukocyte scintigraphy

- Early accumulation in bone marrow
- Late accumulation in site of infection
- Incongruence between early and late images is indicative of infection (as in conventional LS/BMS)

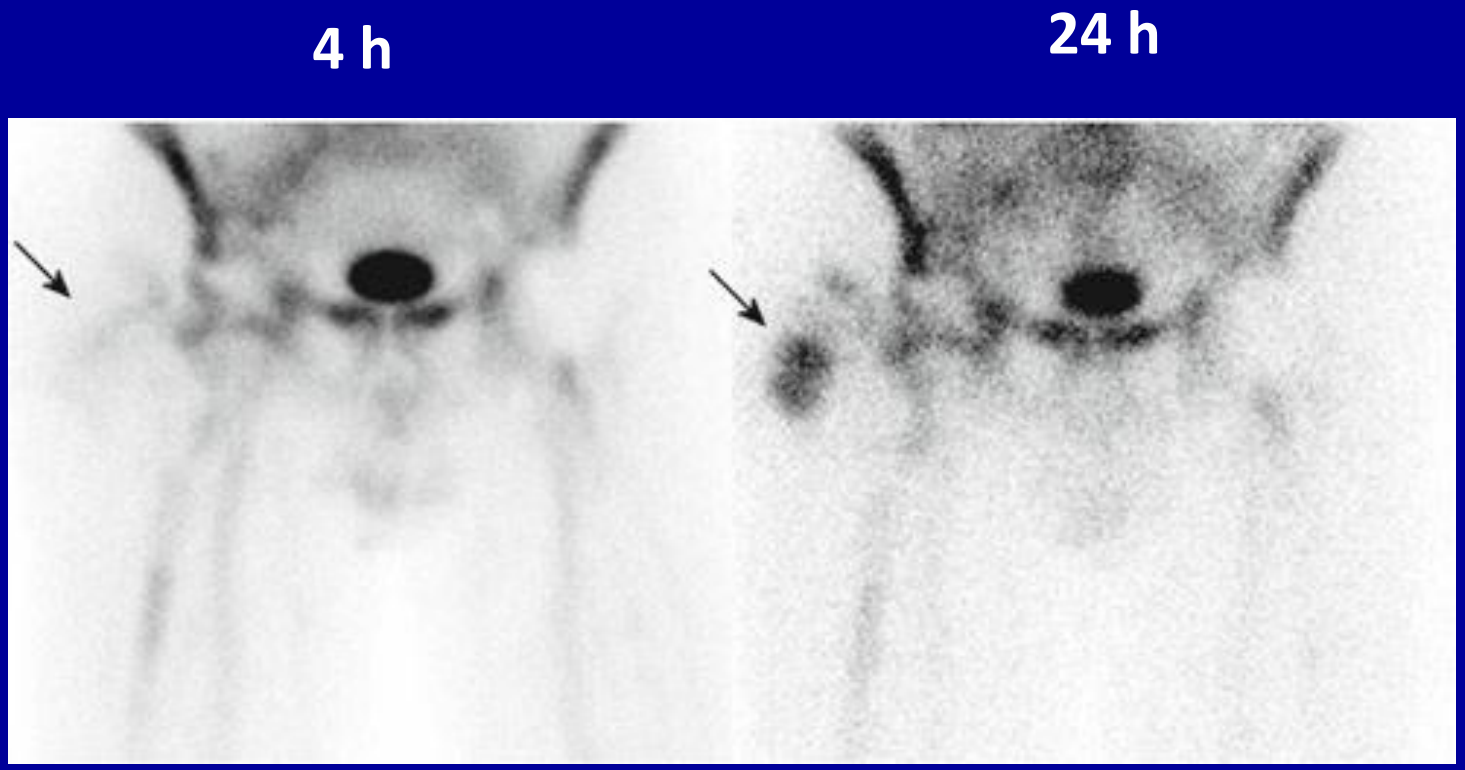
# Dual time leukocyte scintigraphy

- after 4-6h and 20-24 h
- improved sensitivity and specificity

- sensitivity: 1) hip prosthesis 83% (50%)
  2) knee prosthesis 100% (87%)

- specificity: 1) hip prosthesis 100% (90%)
  2) knee prosthesis 82% (77%)

# Labelled leukocyte




**Infected right hip replacement**

4-h (left) and 24-h (right) labelled leukocyte images.
The abnormal labelled leukocyte activity (arrows) is seen clearly only on the later images.

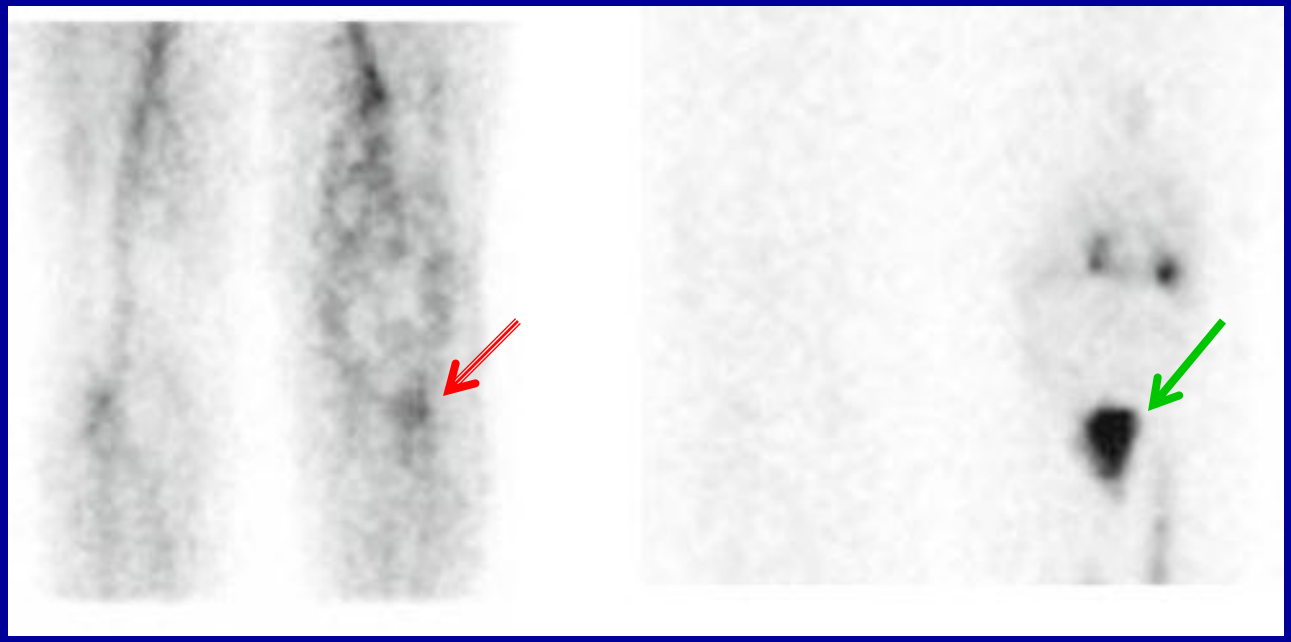
# 5. Antigranulocyte scintigraphy (CGS)

- In vivo labelled leukocyte
- Granuloscint/ Scintimun®
- Sulesomab/ LeucoScan®
- Monoclonal G1 murine immunoglobulin and 50-kDa fragment antigen binding (Fab) portion
- Binds to the antigen NCA 95 i NCA 90 present on acitvated leukocytes
- Possibility of allergic reaction!

# Antigranulocyte scintigraphy -**Scintimun**

30 min.

20 h



**Infected left knee replacement after revision of the tibial component 1 year earlier**

Antigranulocyte antibody scintigraphy: on the **early** image there is faint focal labelled granulocyte activity at the proximal tibia (arrow) and mild diffuse labelled granulocyte activity in the synovium of the knee joint; but on the **20-h** image, there is persistent but now intense focal uptake at the proximal tibia (arrow), probably localized in the soft tissues near the prosthesis itself, indicating an infected knee prosthesis

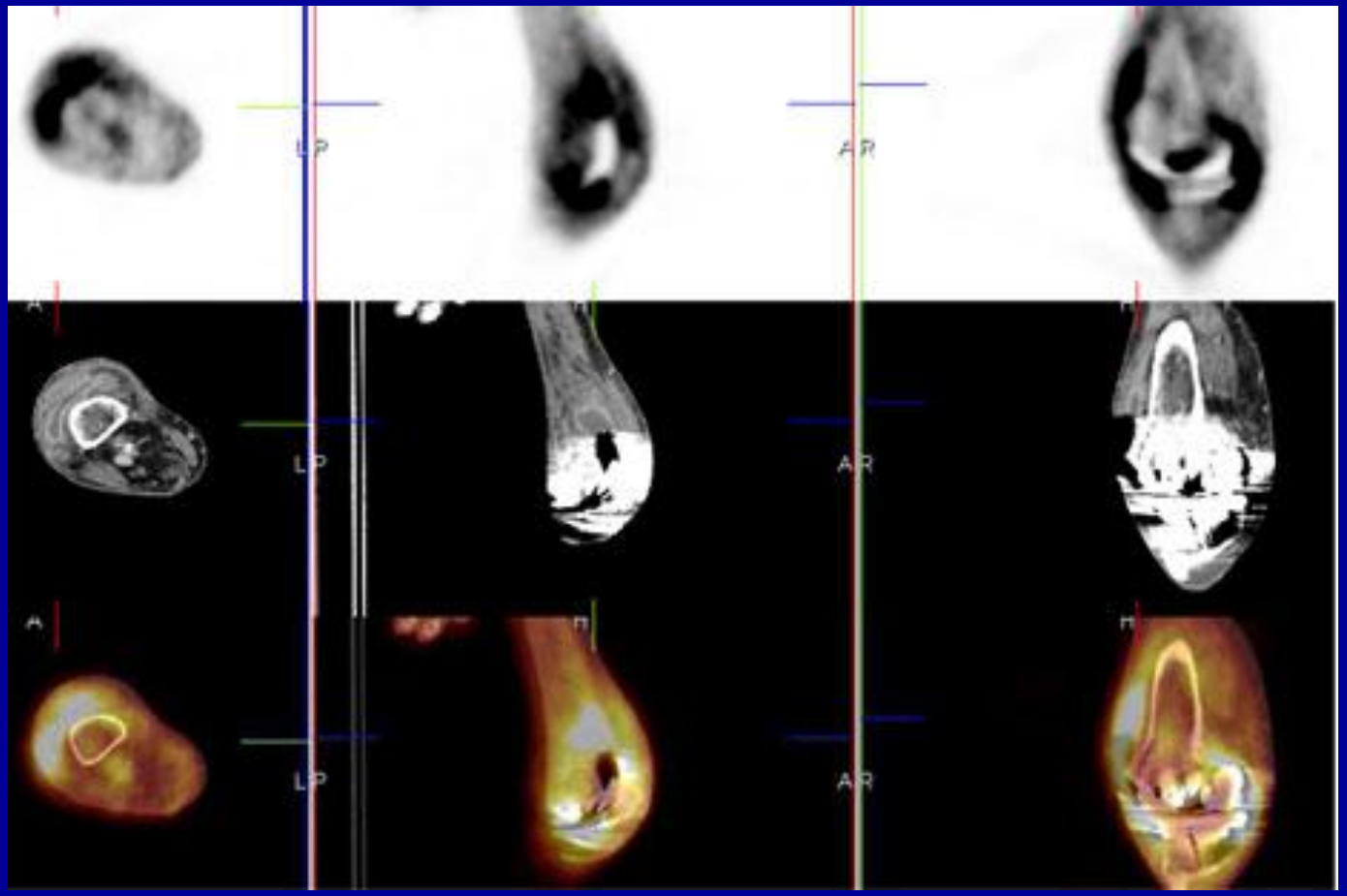
# 6. FDG PET

- $^{18}$F- fluorodeoxyglucose
- Accumulates at the site of  infection
- Improved spatial resolution, imaging completed after 2-3 h
- PET/CT
- Activated leukocytes have higher glucose consumption
- Increaseg periprosthetic uptake during 6 months after insertion

FDG PET

LD CT

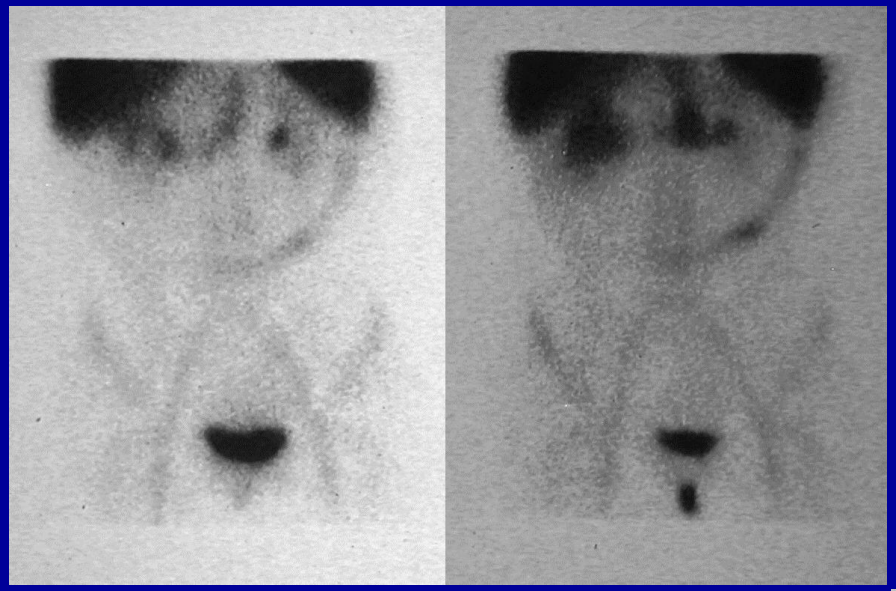
PET/CT



# Infected 4-month-old right knee replacement

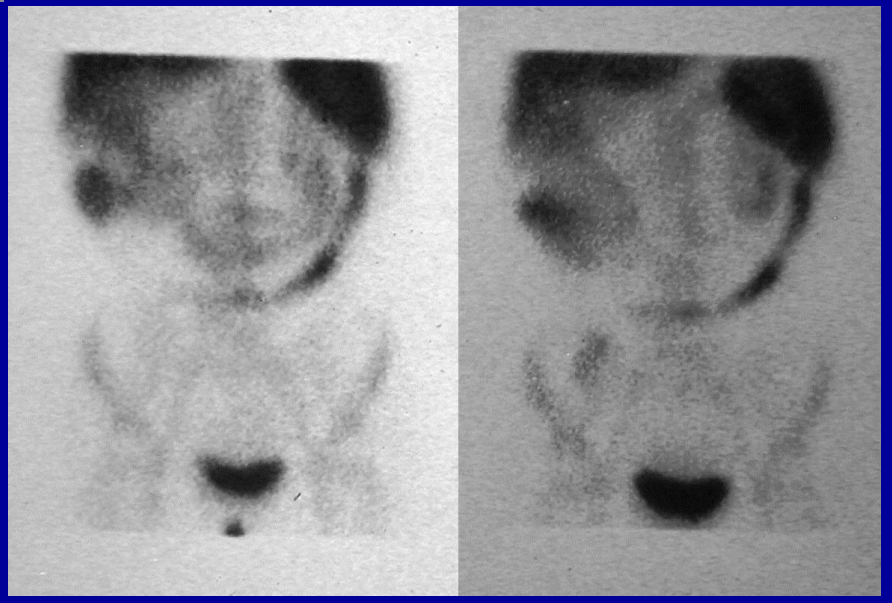
Patient with persistent elevated inflammatory parameters after recent total knee arthroplasty was sent for FDG PET/CT. **Diffuse pathological uptake** around the soft tissues and the knee joint, probably indicating an acute infected knee arthroplasty. Intraoperative findings revealed gross purulence and cultures grew S. aureus. Note presence of metal-induced CT artefacts.

# Inflammatory bowel disease (IBD)



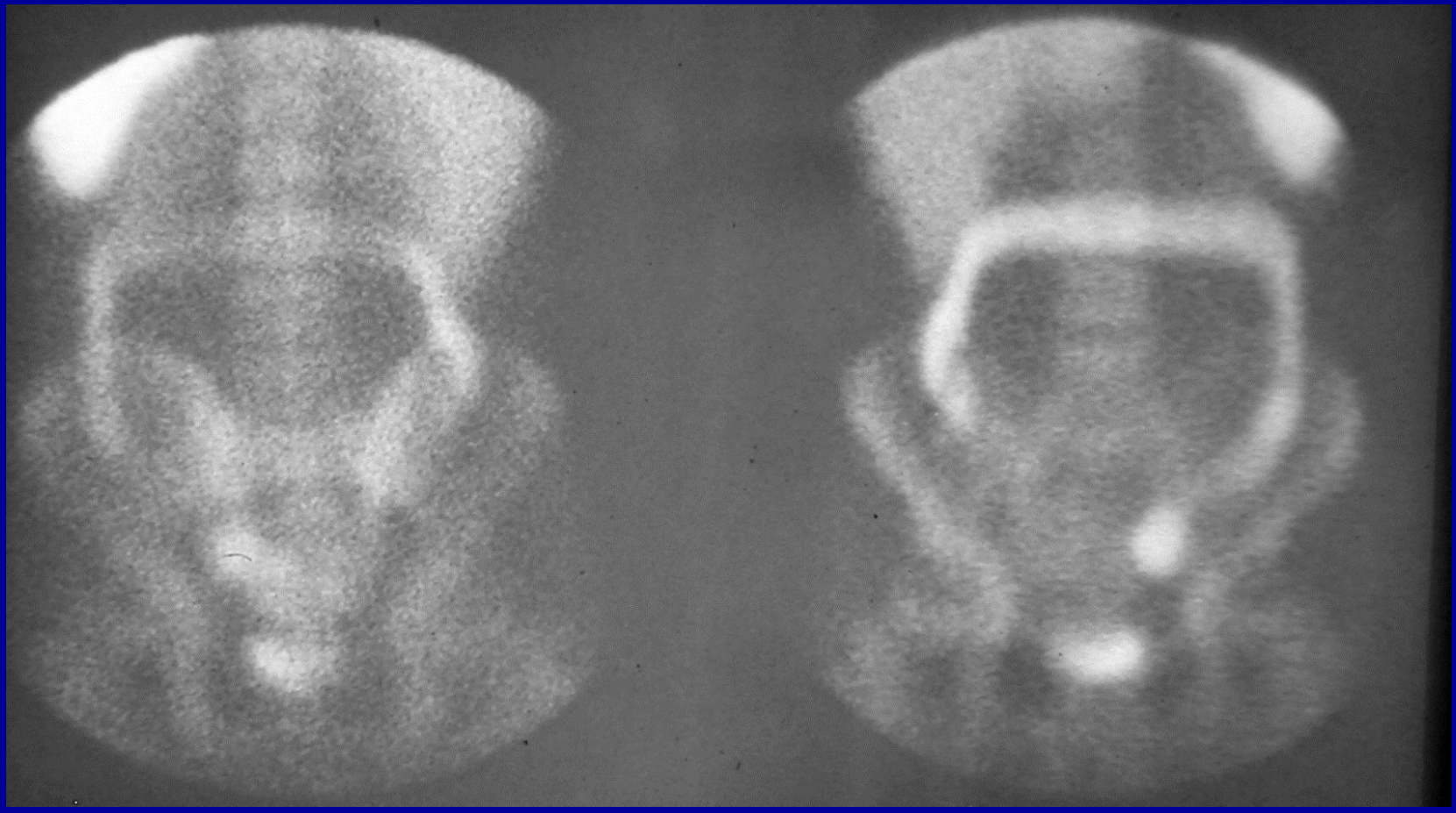
30 min 60 min

120 min 180 min



Tc-99m-HMPAO- labeled leukocytes- Mb Crohn

# Tc-99m-HMPAO- labeled leukocytes- Mb Crohn



PA AP

Tc-99m-HMPAO- labeled leukocytes- Mb Crohn